PREDICTIVE VALUE OF UMBILICAL CORD BLOOD BILIRUBIN AND ALBUMIN FOR SIGNIFICANT HYPERBILIRUBINEMIA IN ABO INCOMPATIBILITY

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MAY 2018

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I hereby solemnly declare that the dissertation titled "**Predictive value of umbilical cord blood bilirubin and albumin for significant hyperbilirubinemia in ABO incompatibility**" has been prepared by me under the guidance of **Prof Dr.P.Selvakumar MD.,** ASSOCIATE PROFESSOR, DEPARTMENT OF PEDIATRICS, THANJAVUR MEDICAL COLLEGE, THANJAVUR. This is submitted to THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY, CHENNAI, in partial fulfillment of the requirement for the degree of DOCTOR OF MEDICINE (PEDIATRICS) (BRANCH VII).

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CONTENTS

LIST OF TABLES

LIST OF FIGURES

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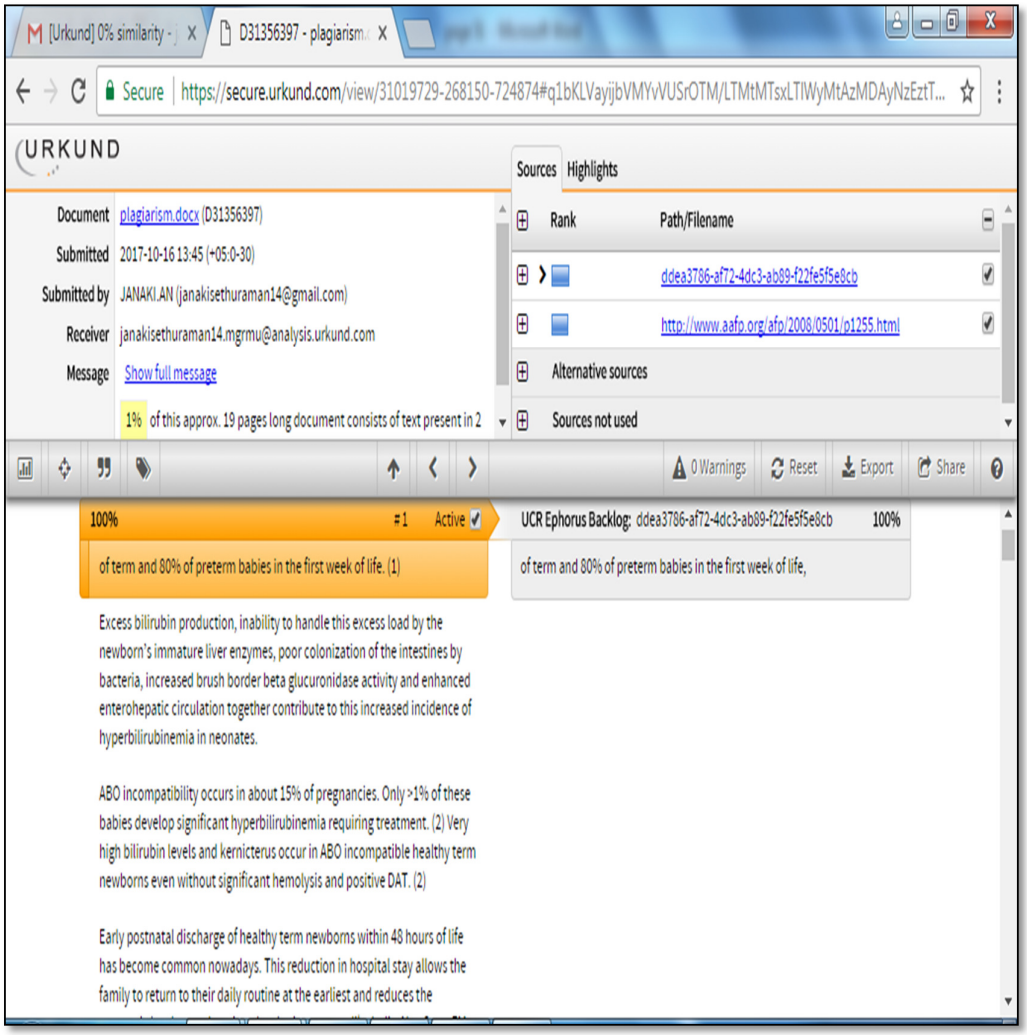
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ABO incompatibility occurs in about 15% of pregnancies. Only >1% of these babies develop significant hyperbilirubinemia requiring treatment. (2) Very high bilirubin levels and kernicterus occur in ABO incompatible healthy term newborns even without significant hemolysis and positive DAT. (2)
Early postnatal discharge of healthy term newborns within 48 hours of life has become common nowadays. This reduction in hospital stay allows the family to return to their daily routine at the earliest and reduces the

CERTIFICATE – II

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INTRODUCTION

The most common clinical abnormality in the neonatal period is neonatal hyperbilirubinemia affecting 60% of term and 80% of preterm babies in the first week of life. (1)Excess bilirubin production, inability to handle this excess load by the newborn's immature liver enzymes, poor colonization of the intestines by bacteria, increased brush border beta glucuronidase activity and enhanced enterohepatic circulation together contribute to this increased incidence of hyperbilirubinemia in neonates.

ABO incompatibility occurs in about 15% of pregnancies. Only <1% of these babies develop significant hyperbilirubinemia requiring treatment. (2) Very high bilirubin levels and kernicterus occur in ABO incompatible healthy term newborns even without significant hemolysis and positive DAT. (2)

Early postnatal discharge of healthy term newborns within 48 hours of life has become common nowadays. This reduction in hospital stay allows the family to return to their daily routine at the earliest and reduces the economic burden on them in a developing country like

India.Also Carty EM and Bradley CF in their study, “A randomized, controlled evaluation of early postpartum discharge”, found that mothers who were discharged from the hospital earlier were significantly more satisfied with the care and had higher exclusive breast feeding rates than the late discharge group. While those mothers in the late discharge group scored higher on measures of depression and lower in confidence.

However, neonatal jaundice, the commonest cause for readmission of newborns to hospital goes unnoticed in those discharged early. (3,4) American Academy of Pediatrics mandates a follow-up visit after 48 to 72 hours of discharge for all neonates who were discharged before 48 hours of life to look for any significant jaundice and other problems.(5) But such follow-up is not feasible in all cases in our country due to parental noncompliance and ignorance.

Kernicterus is an irreversible tragedy, which results in mortality and severe long-term morbidity. It comes under the ‘Never Events’ in the USA.(6) Kernicterus is essentially preventable as phototherapy has a definite risk reduction for bilirubin levels more than 20mg/dl.(7,8)

Many factors have been identified to increase the risk of developing significant hyperbilirubinemia in newborns to necessitate treatment like blood group incompatibility, cephalhematoma, significant bruising, injuries, history of neonatal jaundice in previous sibling and pre-discharge TSB or TcB in high risk zone. Though our understanding of neonatal hyperbilirubinemia has improved in the recent years, we are still not able to precisely predict those babies at risk of developing significant hyperbilirubinemia.

Albumin binds in equimolar concentrations with bilirubin and free bilirubin levels in serum increase at times of low serum albumin concentration. Similar correlations between umbilical cord serum bilirubin and neonatal hyperbilirubinemia also have been discussed for many years now.

In as early as 1960 Robinson et al. reported that cord bilirubin levels above 3mg/dl were highly suggestive of ABO disease. (9) In 1977, Risemberg et al. reported in their study that infants with ABO incompatibility and cord bilirubin levels greater than 4mg/dl are at increased risk of hyperbilirubinemia and that frequent reevaluation is

mandatory. (10) In 1989 Aage Knudsen in his study, found that 85% of babies became jaundiced, if cord bilirubin was above 2.3mg/dl and 57 % of these jaundiced babies required phototherapy. (11)

Since then many researchers studied the correlation between the umbilical cord blood bilirubin and albumin in predicting significant neonatal hyperbilirubinemia. However no study has established a single cut off value for umbilical cord serum bilirubin and albumin especially in ABO incompatibility to allow us to predict at birth those babies who will develop significant hyperbilirubinemia to require therapeutic intervention.

Thus the present study was conducted to evaluate the predictive ability of the umbilical cord blood bilirubin and albumin for significant neonatal hyperbilirubinemia in ABO incompatibility.

REVIEW OF LITERATURE

One of the most biologically active end-products of heme catabolism is bilirubin. It has a propensity to deposit in the skin and mucous membranes, producing easily visible yellowish discoloration – jaundice (French *jaune* -yellow) or icterus (Greek *ictero*). As long as the processes of bilirubin production and elimination are balanced, only a moderate degree of jaundice develops which does not harm an otherwise healthy term newborn.

In rare occasions, when bilirubin production exceeds the body's capacity to eliminate bilirubin, it deposits in the brain to produce Transient or Acute Bilirubin Encephalopathy and Chronic Bilirubin Encephalopathy with permanent neurological damage called Kernicterus.

BILLIRUBIN METABOLISM

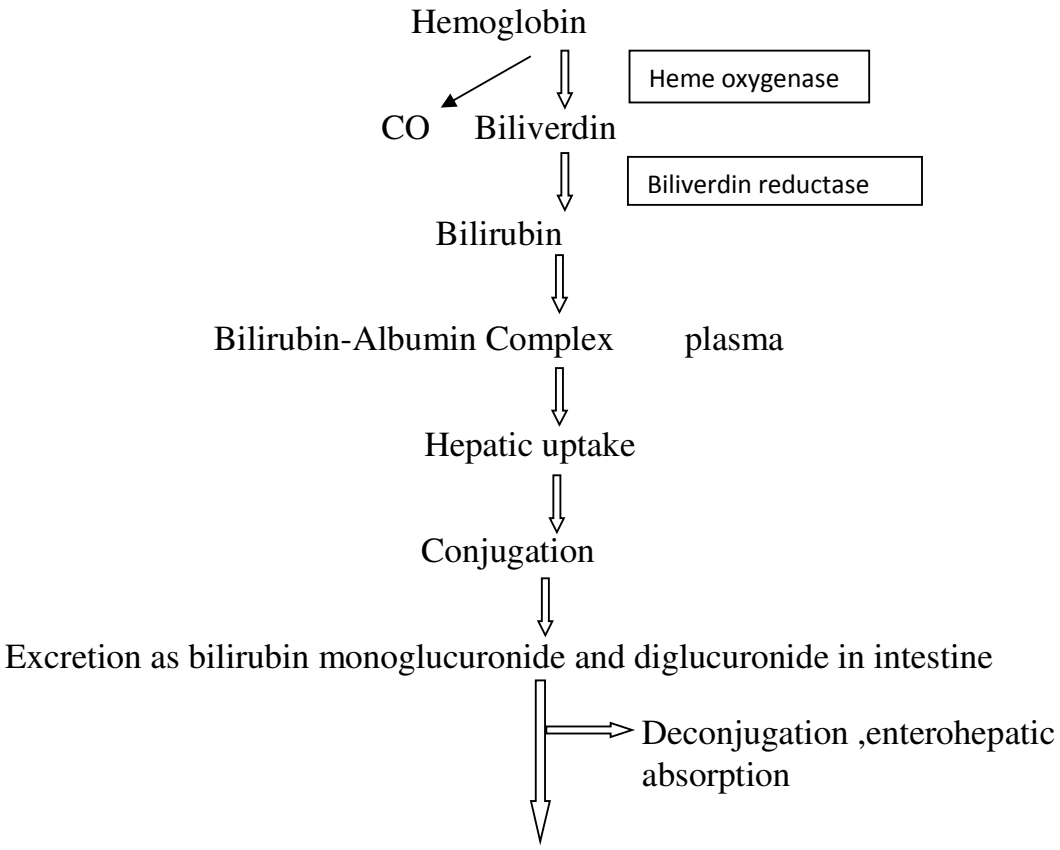
Steps in bilirubin metabolism:

- Bilirubin production
- Transport of bilirubin in plasma

- Hepatic uptake
- Conjugation of bilirubin
- Excretion
- Enterohepatic absorption

BILIRUBIN METABOLISM

Reticuloendothelial system



BILIRUBIN PRODUCTION

Bilirubin is produced from degradation of heme from senescent RBCs and other hemoproteins like, cytochromes and catalase. Causes for excess production in newborns are

- Shortened RBC lifespan (70-90days)
- Large pool of hematopoietic tissue which was essential for intrauterine life
- Increased turnover of cytochromes in newborns

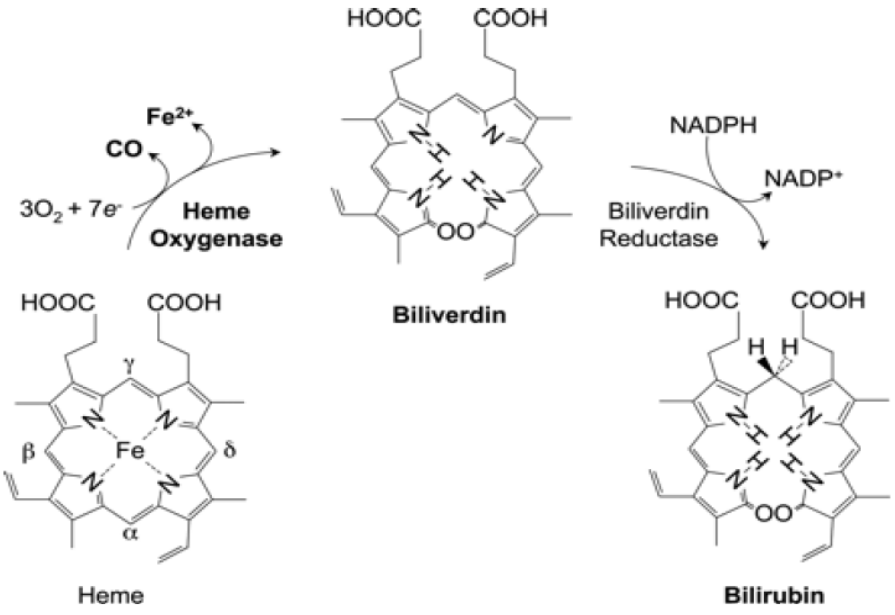


Figure 1: heme to bilirubin

The porphyrin ring structure in heme is opened by heme oxygenase at its alpha methylene bridge to produce biliverdin ix α. This water-soluble nontoxic intermediate pigment billiverdin ix α is the excretory product in amphibians, reptiles and birds. In mammals, billiverdin ix α is reduced by biliverdin reductase to produce bilirubin ix α, the only toxic isomer of bilirubin and smaller amounts of nontoxic bilirubin ix β and ix δ isomers.

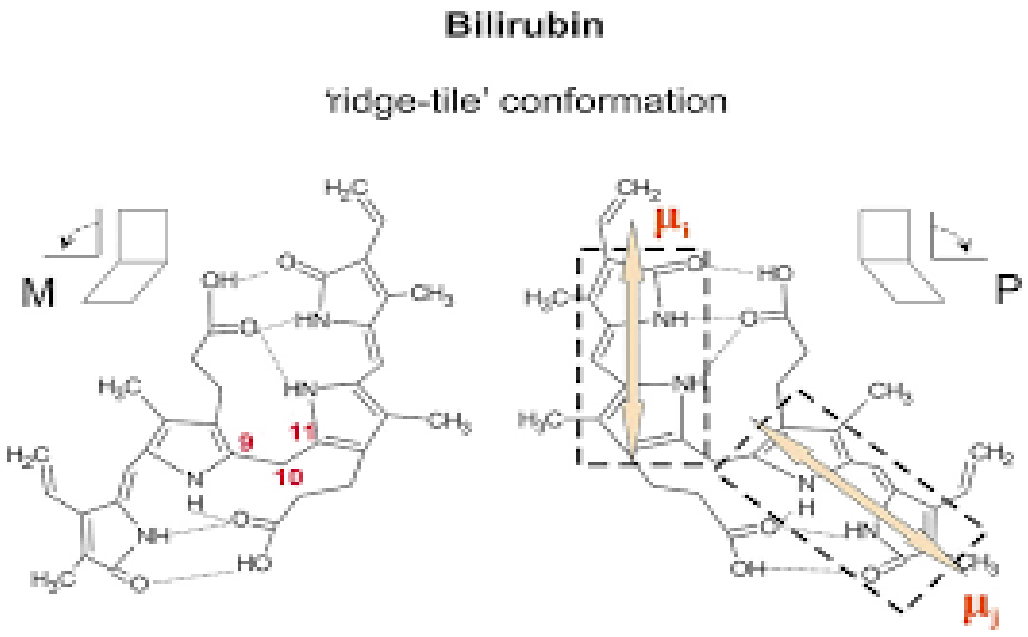


Figure 2: Bilirubin ix α – preffered conformation

One possible explanation for the production of this potentially neurotoxic byproduct of heme in mammals is that, bilirubin serves as an antioxidant, most needed for a newborn with immature antioxidant systems.

The bilirubin molecule is partially folded at its mid-methylene bridge, which makes it virtually insoluble in water and lipophilic enabling it to cross cell membranes and biological barriers like placenta and blood brain barrier.

TRANSPORT OF BILIRUBIN IN PLASMA

Unconjugated bilirubin upon release into the circulation rapidly binds with albumin. Each gram of albumin binds 7 - 8 mg/dl of unconjugated bilirubin. The lower plasma binding capacity of newborns for bilirubin can be explained partly by reduced serum albumin concentrations in newborns compared to adults and partly by reduced molar binding capacities of albumin. The unbound bilirubin in plasma is

the one toxic to the neurons. Thus, albumin binding to bilirubin is important in determining bilirubin toxicity to brain.

Bilirubin exists in 4 different forms in plasma

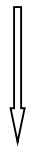
- Unconjugated bilirubin that is reversibly bound to albumin – major portion – gives indirect reaction with diazo reagent
- Free or unbound bilirubin – minute fraction – gives indirect reaction with diazo reagent
- Monoglucuronides and diglucuronides effluxed from hepatocytes – gives directreaction with diazo reagent
- Conjugated bilirubin covalently bound to albumin – δ bilirubin - measured by newer techniques.

HEPATIC UPTAKE OF BILIRUBIN

Bilirubin dissociates from albumin for transport in to hepatocytes. It is transported across the hepatocyte membrane by carrier mediated diffusion and organic anion transporter protein (OATP). Bilirubin is bound to glutathione-s-transferase A (ligandin B) and Z protein.

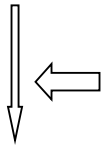
CONJUGATION OF BILIRUBIN

Bilirubin – ligandin complex – transported to endoplasmic reticulum



UDP Glucuronosyl transferase

Bilirubin monogluronide



+ Another molecule of bilirubin glucuronide

Bilirubin digluronide

Bilirubin ix α is conjugated with glucuronic acid at the propionic acid groups resulting in formation of water- soluble bilirubin mono- and di-glucuronides which can excreted in the bowel.

In newborns, mono-glucuronide bililrubin conjugate forms the predominant portion. In term newborns, the immature liver has a UGT activity of about only 1 % of the adult. This is the one of the main reasons for neonatal hyprbilirubinemia. Until 3 months of age, the UGT activity increases at an exponential rate to reach adult levels.

EXCRETION OF BILIRUBIN

The water-soluble bilirubin conjugates incorporated in micelles containing bile acids, phospholipids and cholesterol are excreted by an energy dependent process against a concentration gradient. As a result, bilirubin concentration in bile is 100-folds more than that of hepatocyte cytoplasm.

In adults, hepatic excretion of bilirubin is the rate-limiting step in hyperbilirubinemia. In newborns, hepatic uptake of bilirubin and conjugation are more restrictive than hepatic excretion.

ENTEROHEPATIC ADSORPTION

In intestines, the relatively unstable conjugated bilirubin is readily hydrolyzed to unconjugated bilirubin. This unconjugated bilirubin readily traverses the intestinal mucosa.

Causes for increased enterohepatic circulation in newborn:

- Lack of bacterial flora in the bowel, which converts bilirubin to urobilirubinogen.

- High mucosal β-glucuronidase activity.
- Predominance of monogluronide bilirubin conjugates compared to adults.

FETAL HANDLING OF BILIRUBIN:

During the fetal life, unconjugated bilirubin is transported across the placenta to mother. Thus, even in cases with severe intrauterine hemolysis, the degree of anemia exceeds hyperbilirubinemia at birth. Placenta is not permeable to conjugated bilirubin, which explains the presence of jaundice at birth in conjugated hyperbilirubinemia. Bilirubin also diffuses across the amniotic membrane and increases in severe hemolytic diseases in the fetus, allowing it to measured by both invasive and noninvasive methods to aid in the management of Rh erythroblastosis.

PHYSIOLOGICAL HYPERBILIRUBINEMIA

In contrast to older children and adults, elevations in unconjugated bilirubin level occurs in almost every newborn. This phenomenon of "normal" increase in total bilirubin should be distinguished from the pathologic state and the term "*physiologic bilirubinemia"* can be used rather than hyperbilirubinemia.(12)

At birth when placenta is removed, total bilirubin increases during the first few days of life and reaches a peak at 5th day of life. Causes for this physiologic bilirubinemia in newborns are varied which include,

- Physiologic polycythemia – high RBC volume/kg body wt
- Shorter RBC life span
- Increased ineffective erythropoieisis
- Deficiency of hepatic proteins – ligandin, Y,Z acceptor
- Reduced UDP glucuronosyl transferase activity- the central rate limiting step
- Reduced gut motility and paucity of gut flora
- High β glucuronidase enzyme activity

In term neonates the total bilirubin level rises progressively from a mean of 2mg/dl in cord blood to a mean peak of 5 – 6mg/dl by 48 – 120 hours of life. Then it falls gradually by 7^{th} to 10^{th} day of life.

CAUSES OF NEONATAL HYPERBILIRUBINEMIA

i) OVER PRODUCTION

(1) Fetomaternal blood group incompatibility

(2) Heriditary spherocytosis, elliptocytosis

(3) G6PD and other enzyme deficiency

(4) Acquired hemolysis

ii) METABOLIC CAUSE

(1) Galactosemia

(2) Crigler-najjar syndrome

(3) Gilbert disease

(4) Hypothyroidism

(5) Infant of diabetic mother

(6) Prematurity

iii) OTHER CAUSES

(1) Sepsis

(2) Intrauterine infections

(3) Respiratory distress syndrome

(4) Certain ethnic race – Chinese, American Indian, Korean, Japanese infants

ABO INCOMPATIBILITY

The anti-A and anti-B antibodies, which are, IgG type, present in mothers with O blood group, cross the placenta and attach to A or B blood group fetus' RBC membrane antigens. These IgG coated RBCs are hemolysed in the reticuloendothelial system by Fc-receptor-bearing cells.

With a fall in the incidence of Rh isoimmunisation due to better immune prophylaxis, Direct Coombs Test positive ABO incompatibility has become the commonest cause of severe neonatal hyperbilirubinemia. ABO fetomaternal incompatibility occurs in about 15%of pregnancies.

About one third of babies with blood group A or B born to a mother with blood group O, show positive DAT.(13). Chen JY and Ling UP's study, only <26% of the babies with ABO incompatibility had positive DAT.(2) Studies have shown varying incidences of hyperbilirubinemia in DAT positive babies. In a study by Mebere A and Johansen KB, total bilirubin greater than 12.8mg/dl was found in only 20 % of babies with a positive DAT, (13) whereas another study by Kaplan M et al found that 19.6% of DAT positive babies required phototherapy.(14)

In babies with ABO incompatibility and DAT negative also cause early and rapidly progressive jaundice. This in part is explained by, an interaction with polymorphisms for the $(TA)_7$ sequence in the promoter of the gene coding UGT1A1.(14)

LABORATORY EVALUATION OF JAUNDICED INFANT

Table 1: laboratory evaluation of the jaundiced infant ≥35 weeks of gestation(7)

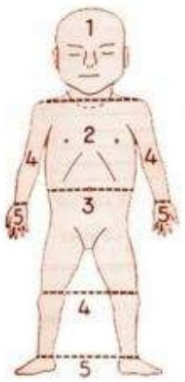
INDICATIONS	ASSESSMENTS
Jaundice in first 24 hour	TcB and/or TSB
Jaundice appears excessive for age	TcB and/or TSB
infant receiving phototherapy/ TSB rising rapidly	Blood type, Coombs test CBC, smear Direct bilirubin
TSB approaching exchange levels or not responding to phototherapy	Reticulocyte count, G6PD, albumin, $ETCO_c$
Elevated direct bilirubin	Urinalysis and urine culture Evaluate for sepsis
Jaundice persisting beyond 3 weeks of life	TSB and direct bilirubin If direct high – evaluate for causes for cholestasis Thyroid and galactosemia screen

LABORATORY METHODS OF BILIRUBIN ESTIMATION

❖ NON INVASIVE:-

➢ Clinical – cephalocaudal progression(kramers rule)(15)

Schema for grading extent of jaundice



Grade	Extent of Jaundice
0	None
1	Face and neck only (4 - 6 mg/dl)
2	Chest and back (6 - 8 mg/dl)
3	Abdomen below umbilicus to knees 8 - 12 mg/dl)
4	Arms and legs below knees (12 - 14 mg/dl)
5	Hands and Feet (>15 mg/dl)

Figure 3: Grading of jaundice by visual inspection

➢ Icterometer

Figure 4: Icterometer

Figure 5: Comparing the baby's skin colour with standard in the icterometer

- Transcutaneous bilirubinometer

Figure 6: Transcutaneous bilirubinometer

Figure 7: Measuring bilirubin by Transcutaneous bilirubinometer

This method uses reflectance photometry to detect total bilirubin levels. Bilichek and JM-103 jaundicemeter are currently available. These devices can be used as potential predischarge tools.(16) The disadvantages being it is less reliable in

- Values >257micromol/l
- Dark skinned babies
- Preterm
- Low birth weight babies
- During and after phototherapy.

❖ INVASIVE METHODS

- Capillary bilirubin estimation by spectrophotometry
- Filter paper with bilirubinometer
- Laboratory estimation
  - Diazo reaction / Van den bergh reaction – in an aqueous solution, Ehrlich diazo reagent reacts with direct bilirubin in serum to give a pink to reddish purple coloured azobilirubin read at one minute. In 50% methyl alcohol solution, it reacts with total bilirubin to form pink to reddish purple coloured compound read at 30 minutes.
  - Bilirubinometer –
    - Direct spectrophotometry
    - The jendraussik grof method
    - The Malloy Evelyn method
  - High pressure liquid chromatography – the gold standard, relatively rapid and quantifies all 4 fractions of bilirubin

- Enzymatic method-
    - Peroxidase method
    - Peroxidase diazo method
- Simple calorimetric method

END-TIDAL CARBON MONOXIDE MEASUREMENTS

Heme is broken down by heme oxygenase ezyme into euimolar quantities of carbonmonoxide and biliverdin. This measurement of CO in end –tidal breath with a portable device can be used as a bedside index of in vivo heme degradation and bilirubin production and hence, hemolysis.(17)

BILIRUBIN TO ALBUMIN MOLAR RATIO (BAMR)

The molar ratio of bilirubin to albumin correlates with unconjugated bilirubin levels and can be used as a surrogate for unbound bilirubin.(18) The BAMR can be used as an adjunct to TSB measurement in determining the need for exchange transfusion.(7)

SEQUELAE OF UNCONJUGATED HYPERBILIRUBINEMIA

The unconjugated bilirubin passively diffuses across the blood brain barrier. Disruption of blood brain barrier by conditions like meningitis, hypertonicity of serum and hypoxemia, all increase the permeability of BBB to bilirubin and other toxic products.

It causes staining and necrosis of neurons in the basal ganglia, hippocampal cortex, subthalamic nuclei, and cerebellum. It accumulates in the cytoplasm and results in increased oxidative stress, decreased neuronal proliferation and presynaptic neurodegeneration at the central glutaminergic synapses.(19) However, a level of serum bilirubin does not always correlate with development of bilirubin induced neuronal damage, as kernicterus has been reported in cases even without a very high serum bilirubin.

Albumin binds bilirubin in vivo preventing it from crossing blood brain barrier. The bilirubin-binding capacity of albumin is thought to be decreased in sick neonates.(20) Also these babies have a relatively low serum albumin levels. Both of these factors may increase the risk of

kernicterus at lower total serum bilirubin in sick neonates. Various techniques have been proposed to measure bilirubin binding capacity of albumin. However, their application and interpretation in clinical management are not generally accepted.

The clinical manifestations of bilirubin-induced neurologic dysfunction (BIND) is classified as

- Acute bilirubin encephalopathy
- Chronic permanent sequelae of BIND – Kernicterus

TRANSIENT ENCEPHALOPATHY OR ACUTE BILIRUBIN ENCEPHALOPATHY

In the first week of life, the manifestations include

- Lethargy
- Hypotonia
- Poor suck

At the end of first week of life, the second phase sets in which is characterized by

- ❖ Hypertonia
- ❖ Opisthotonus
- ❖ High pitched cry
- ❖ Fever
- ❖ Seizures

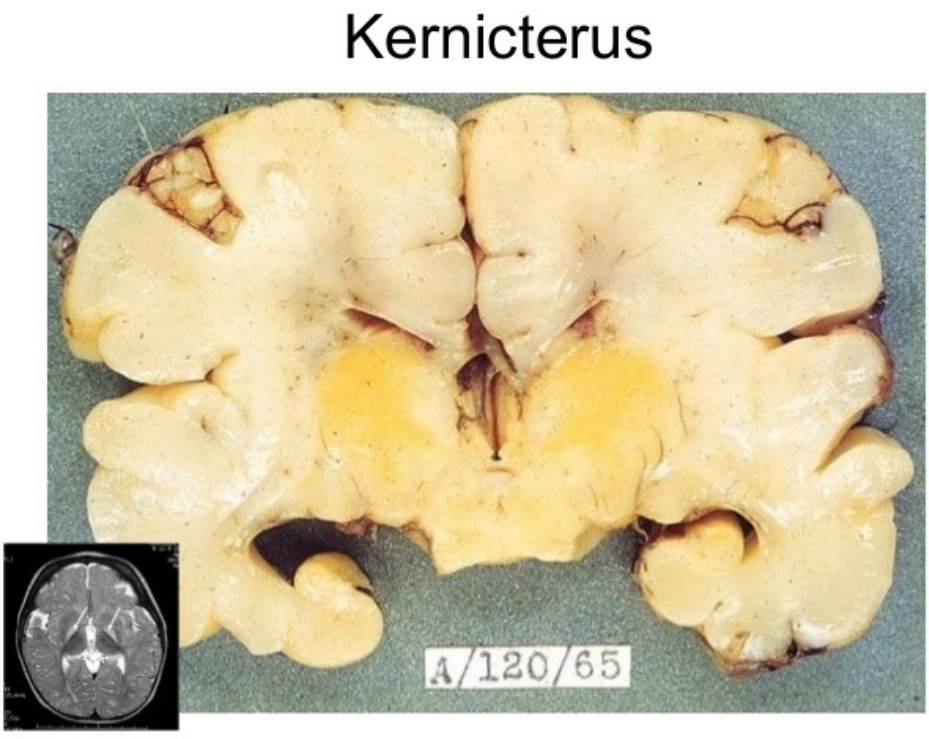


Figure 8: Macroscopic appearance of brain in an extremely low-birth weight infant with kernicterus

The onset of hypertonia and opisthotonus indicates poor prognostic signs and coincide with peak serum bilirubin levels. Intervention in the form of feeding support, phototherapy and if necessary, exchange transfusion can prevent the evolution of long term damage.(21)

LATE SEQUELAE

- The longterm features of bilirubin encephalopathy includes extrapyramidal disturbances
- auditory impairment
- upward gaze palsy
- athetoid cerebral palsy

A characteristic MRI pattern in brain has been described in cases of kernicterus. The presence of high-intensity areas in the postero-medial border of the globus pallidus on T2 weighted imaging is considered most sensitive finding.(22)

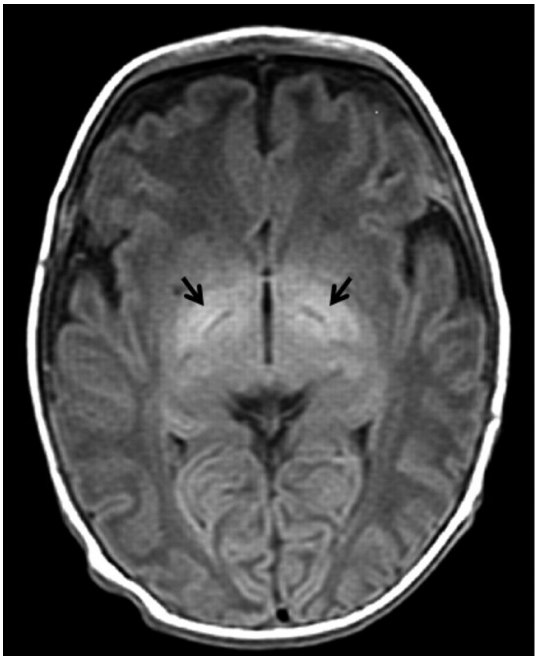


Figure 9: MRI brain showing hyperintensity in globus pallidus in T2 weighted imaging.

AUDITORY NEUROPATHY SPECTRUM DISORDER

Auditory pathway is the most sensitive part of the central nervous system to bilirubin induced toxicity. Permanent sequelae may result from only moderately elevated total serum bilirubin levels, manifesting clinically as Auditory Neuropathy Spectrum Disorder.(23)

Auditory Brainstem Response (ABR) is the gold standard for the diagnosis of BIND.(24) ABR shows reduced amplitudes and increased latencies of ABR waves III and IV.

SCREENING FOR JAUNDICE AND PREVENTION OF ACUTE AND LONG TERM SEQUALAE OF HYPERBILIRUBINEMIA – A "NEVER EVENT"

"Never events" are entirely preventable serious incidents with a potential to cause patient harm or death. Kernicterus has been enlisted as one of the Never Events in UK by National Institute of Health and Clinical Excellence (NICE) and in US by National Quality Forums(6).

National institutes of various countries (AAP, NICE – UK, etc) have proposed guidelines for screening for screening of significant neonatal hyperbilirubinemia and treatment thresholds.

American Academy of Pediatrics recommends that newborns discharged within 48 hours of life should have a follow-up visit after 2-3 days.(5) The AAP also has developed a resource kit and bilitool a web

based program as a practical instrument for plotting hour specific TSB/TcB measurements.

NICE 2010 reccomends risk assessment in every newborn and review within 48 hours of birth of babies with known risk factors for significant hyperbilirubinemia. NICE has provided a billi-wheel to display the treatment thresholds and assist in precise measurement of baby's age in hours.

A recent meta-analysis showed that infants at risk of severe hyperbilirubinemia in low and middle-income countries are associated with the following maternal and neonatal factors that can be effectively managed with available interventions to curtail the disease burden.(25)

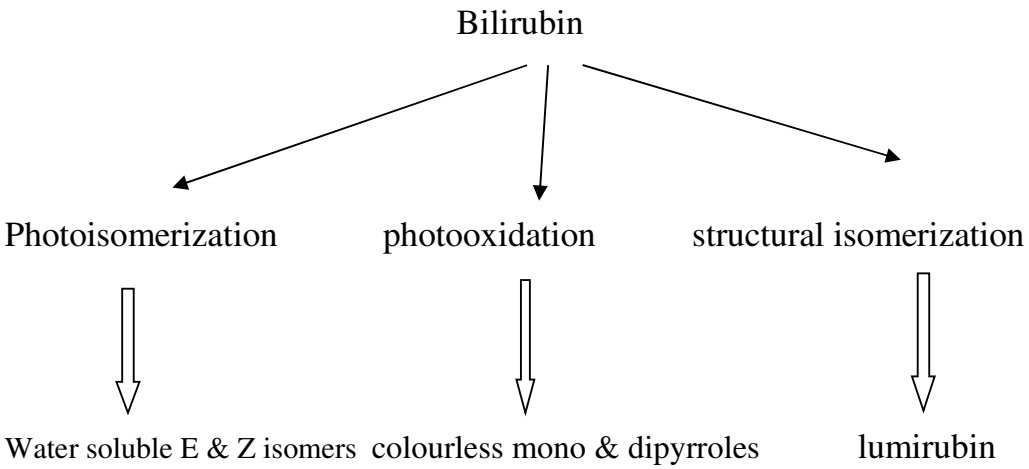
1. primiparity
2. delivery outside the public hospital
3. ABO incompatibility
4. Rhesus hemolytic disease
5. G6PD deficiency
6. UGT1A1 polymorphisms

7. Low gestational age
8. Under weight / weightg loss
9. Sepsis
10. High TcB/TSB

PHOTOTHERAPY

Phototherapy is the most widely used form of treatment of neonatal unconjugated hyperbilirubinemia. It blunts the rise of serum total bilirubin concentration regardless of hemolysis, maturity and skin pigmentation.

MECHANISMS OF ACTION



Blue green light in the range of 460 – 490 nm is used. The absorption of light by bilirubin results in formation of 2 isomers:

- E and Z isomer –
    - Configurational isomer
    - Water soluble, excreted in bile and urine without the need for conjugation.
    - Reversible- revert back to bilirubin rapidly

- Lumirubin –
    - Structural isomer
    - Water soluble, excreted in bile and urine without the need for conjugation.
    - Irreversible
    - Rate limiting step in excretion of bilirubin by phototherapy

Phototherapy results in the formation of excited state bilirubin, which reacts with oxygen to form photo-oxidation products. They play a relatively minor role in photocatabolism of unconjugated hyperbilirubinemia.

Lee KS et al, studied the association between duration of neonatal hospital stay and readmission to hospital. They found that neonates discharged earlier had higher readmissions for conditions that develop after 2-3 days of life especially jaundice and dehydration. They also raised a question whether early discharge of apparently well term neonates is always safe.(25)

M. Jeffrey Maisels and Elizabeth Kringin their study, “Length of hospital stay, jaundice, and hospital readmission”, evaluated the effect of postnatal age at the time of discharge on the risk of hospital readmission with special reference to hyperbilirubinemia. They concluded that babies discharged earlier than 72 hours of life are at more risk for readmission especially due to hyperbilirubinemia.(26)

Keily M, Drum MA and Kessel W studied the risks and benefits of early discharge of mother and the newborn baby. They found that early discharge had a positive effect on the mental status of the mother and better exclusive breast feeding rates at the end of one month though the risk of readmission of the newborn for conditions that manifest after the first 2 days was higher in the early discharge group.(4)

Amar Taksande et al reported that only 2.05% of the newborns with cord blood bilirubin levels less than 2 mg/dl develop significant jaundice and a critical cord bilirubin level of 2 mg/dl in all healthy term newborn had a negative predictive value of 98.7% and that it can be used to predict significant hyperbilirubinemia at birth.(27)

Hamdi et al in their prospective study which included newborns more than 35 weeks gestation found that there is a 91% probability for the need of phototherapy levels for those term and near term newbornswhose umbilical cord serum bilirubin was more than or equal to 2 mg/dl.(28)

Sandeepkumar et al in their prospective study on term healthy newborns found that there is a significant relation between cord serum albumin and hyperbilirubinemia and a cord serum albumin level of less than or equal to 2.8 mg/dl can be used as a risk indicator in predicting the development of neonatal hyperbilirubinemia at birth. While umbilical cord serum albumin level of more than or equal to 3.4 mg/dl was found to be safe for early discharge.(29)

Naharb Z et al in their study, which included both term and preterm newborns, concluded that a critical value of cord blood bilirubin more than 2.5 mg/dl had the high sensitivity (77%) and specificity (98.6%) for predicting neonatal hyperbilirubinemia.(30)

Saltrya R et al in their study "Correlation between cord blood bilirubin level and incidence of hyperbilirubinemia in term newborns" concluded that cord blood bilirubin level of more than or equal to 2.54 mg/dl can predict the development of neonatal hyperbilirubinemia requiring phototherapy. (31)

Zeitoun AA et al in their prospective study "predictive value of umbilical cord blood bilirubin in neonatal hyperbilirubinemia" found that a cord blood bilirubin level of more than or equal to 2.05 mg/dl in late preterm newborn and more than or equal to 2.15 mg/dl in full term newborns to predict the development of significant hyperbilirubinemia.(32)

Trivedi et al in their study found a total cord serum bilirubin level of more than or equal to 2.5 mg/dl to be a risk indicator for developing neonatal hyperbilirubinemia in the first week of life. They also found that 58.53% of babies who developed hyperbilirubinemia had serum albumin level less than 2.8 g/dl.(33)

Bernaldo AJN and Segre CADM in their study, “bilirubin dosage in cord blood: could it predict neonatal hyperbilirubinemia?” concluded that unconjugated bilirubin levels in cord blood of more than or equal to2 mg/dl to be indicative of 53% probability of the need for phototherapy (34)

Meena JK, Singh S, Veema CR and Sharma R in their study “utility of cord blood albumin as a predictor of significant neonatal jaundice in healthy term newborns” found that 95.5% of babies who needed phototherapy to have cord serum albumin levels less than 2.8 g/dl. They also concluded that a cord serum albumin level of more than 3.3 g/dl to be safe.(35)

Venkatamurthy M, Murali SM and Mamatha S in their study “A comparison study: cord serum albumin is compared with cord serum bilirubin as a risk indicator in predicting neonatal jaundice” concluded that cord serum albumin and cord serum bilirubin are equally effective in predicting neonatal jaundice. Also in their study cord serum albumin level of less than 2.8 g/dl had a sensitivity of 95%, specificity of 62.34% and a negative predictive value of 98.97%. While cord serum bilirubin

level of more than or equal to 2 mg/dl had a sensitivity of 100 %, specificity of 61.04% and a negative predictive value of 100%.(36)

Kanchanabat S, Boonyarthipong p and Kreinghirim O in their study "prediction of hyperbilirubinemia in term newborns by umbilical cord blood bilirubin", found that a cut off value of cord serum bilirubin of more than 2.3 mg/dl to have a positive predictive value of 25%, a negative predictive value of 84.3%, sensitivity of 14.6% and a specificity of 91.3%.(37)

Reshad M, Ravichander B and Raghuraman TS in their study "A study of cord blood albumin as a predictor of significant neonatal hyperbilirubinemia in term and preterm newborns" concluded that a cord serum albumin level of less than or equal to 2.8 g/dl can predict significant hyperbilirubinemia in healthy term and preterm newborns.(38)

AIMS AND OBJECTIVE

1. To estimate the levels of bilirubin and albumin in cord blood.

2. To estimate the relationship between cord blood bilirubin and occurrence of neonatal hyperbilirubinemia.

3. To estimate the relationship between cord blood albumin and occurrence of neonatal hyperbilirubinemia.

METHODOLOGY

STUDY PLACE:

Rajah Mirasudhar Hospital attached to Thanjavur Medical College, Thanjavur.

STUDY PERIOD:

February 2017 to August 2017.

STUDY DESIGN:

Prospective study

SAMPLING METHOD:

Purposive sampling

SAMPLE SIZE:

Sample size was calculated using online openepi.com. Keeping the two sided confidence interval as 99% (α=0.99) and power as 90% (β=0.9), the ratio between the groups as 1 and the mean difference between the group as 0.37 with standard deviation of 0.46 the sample size obtained

was 92. Keeping 10% dropout (10% of 92 = ~9) the final sample size was 100 for two groups.

INCLUSION CRITERIA

- Term babies (≥37 completed weeks) of both gender delivered at Rajah Mirasudhar Hospital attached to Thanjavur Medical College, Thanjavur.
- Mode of delivery – normal vaginal delivery / cesarean section
- Birth weight ≥ 2.5 to 4 kg.
- Apgar score ≥ 7/10 at 1 minute
- Study group: babies with blood group A or B born to O positive mothers
- Control group: babies with blood group O positive born to O positive mothers

EXCLUSION CRITERIA

- Preterm
- Rh incompatibility
- At risk of sepsis(as those babies born to mothers with PROM>12 hours)
- Instrumental delivery (vacuum and forceps)
- Birth asphyxia
- Direct hyperbilirubinemia
- Infant of diabetic mother
- Significant congenital anomalies
- Meconium stained amniotic fluid

Informed written consent was obtained from the parents.

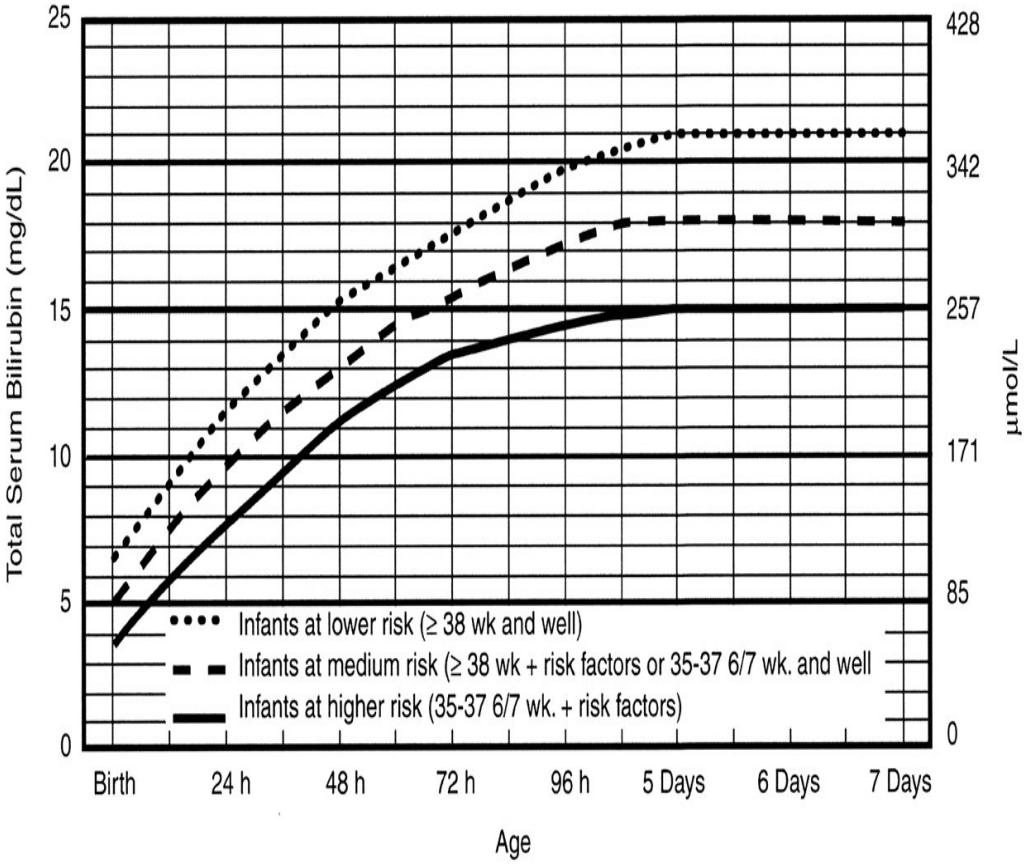
A detailed history including mother's age, maternal complications, medications, family history of neonatal jaundice and type of delivery was obtained by interviewing the mother and from maternal hospital records.

A complete physical examination of the baby was done at birth to assess the gestational age, and to look for the presence of birth trauma, congenital anomalies and cephalhematoma. Apgar score at 1st and 5th minute of life was recorded. 3ml of cord blood was collected at birth for blood grouping, Rh typing and estimation of serum bilirubin and albumin.

The babies were examined daily and looked for the development of jaundice. Serum bilirubin was estimated in all newborns at 24 and 72 hours of life.

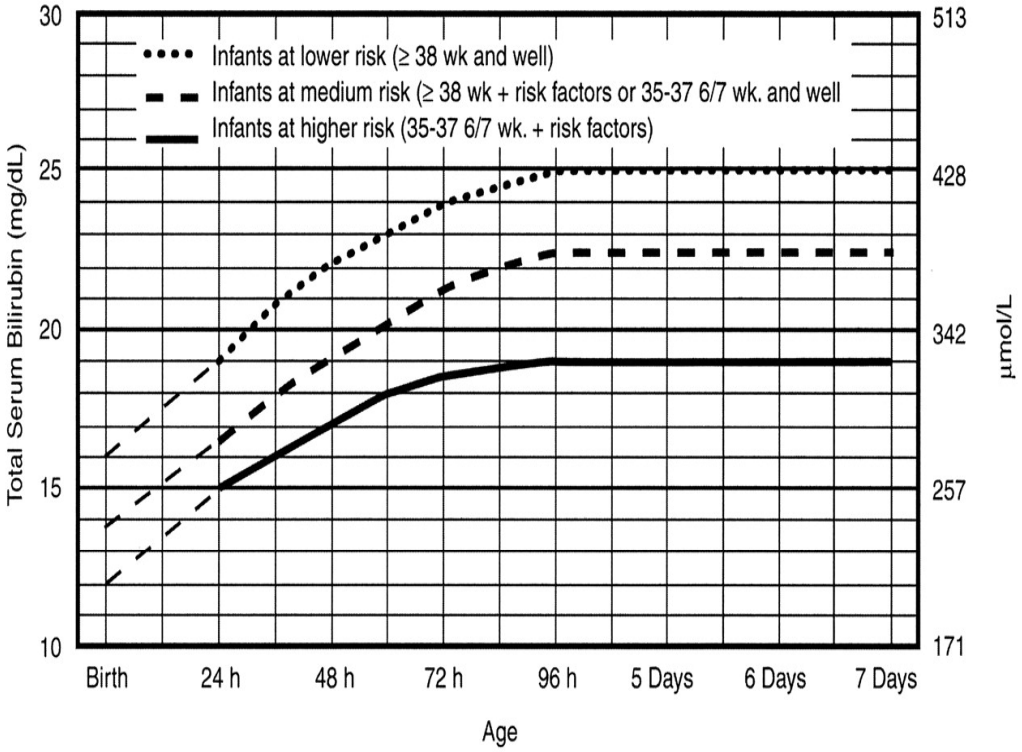
Serum bilirubin was estimated by diazo method using Erba system pack reagent in auto-analyzer. Serum albumin was measured using Erba system pack reagent containing bromocresol green by biuret method.

Babies developing significant hyperbilirubinemia were treated with phototherapy and exchange transfusion as per AAP 2004 guidelines.(5)



- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin.
- Risk factors = isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis, or albumin < 3.0g/dL (if measured)
- For well infants 35-37 6/7 wk can adjust TSB levels for intervention around the medium risk line. It is an option to intervene at lower TSB levels for infants closer to 35 wks and at higher TSB levels for those closer to 37 6/7 wk.
- It is an option to provide conventional phototherapy in hospital or at home at TSB levels 2-3 mg/dL (35-50mmol/L) below those shown but home phototherapy should not be used in any infant with risk factors.

Figure 10: AAP guidelines for phototherapy in hospitalized infants 35 or more weeks' gestation.(39)



- The dashed lines for the first 24 hours indicate uncertainty due to a wide range of clinical circumstances and a range of responses to phototherapy.
- Immediate exchange transfusion is recommended if infant shows signs of acute bilirubin encephalopathy (hypertonia, arching, retrocollis, opisthotonos, fever, high pitched cry) or if TSB is ≥5 mg/dL (85 µmol/L) above these lines.
- Risk factors - isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis.
- Measure serum albumin and calculate B/A ratio (See legend)
- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin
- If infant is well and 35-37 6/7 wk (median risk) can individualize TSB levels for exchange based on actual gestational age.

Figure 11: Guidelines for exchange transfusion in newborns of 35 or more weeks' gestation.(40)

Complete blood count, peripheral smear and direct coombs test were done in all babies who developed significant hyperbilirubinemia.

The development of significant hyperbilirubinemia requiring phototherapy with or without exchange transfusion as per AAP guidelines (39,40) was taken as the major outcome of the study.

The collected data were analysed with IBM.SPSS statistics software 23.0 Version. To describe about the data descriptive statistics, frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significant difference between the bivariate samples in independent groups the unpaired sample t-test was used. The Receiver Operator Characteristic (ROC) curve analysis was used to find the cut-off with sensitivity and specificity for the efficacy of tools.To find the significance in categorical data, Chi-Square test was used. If the expected cell frequency is less than 5 in 2×2 tables, then the Fisher's Exact was used. In all the above statistical tools, the probability value of 0.05 is considered as significant level.

RESULTS

Table 2: Baseline characteristics of study population

S. No	Parameter	Control (n=55)	Cases (n=37)	P value	Statistical test
1	Maternal Age (years)	24.91 ±2.93	26.03 ± 2.98	0.078 (NS)	Unpaired 't' test
2	Sex of the baby				
	Male	25 (45.5%)	21 (56.75%)	0.395 (NS)	Fisher's exact test
	Female	30 (54.5%)	16 (43.25%)		
3	Mode of the delivery				
	Cesarean Section	49 (89.1%)	35 (94.6%)	0.467 (NS)	Fisher's exact test
	Labor Natural	6 (10.9%)	2 (5.4%)		
5	Birth weight of the baby (Kg)	2.9 ± 0.31	2.8 ± 0.29	0.517 (NS)	Unpaired 't' test
6	Gestational age (days)	274 ± 6	275 ± 6	0.195 (NS)	Unpaired 't' test

P<0.05 is considered statistically significant. NS=Nonsignificant

Data were expressed as mean ± SD except sex of the baby and mode of delivery wherein the data are expressed as absolute numbers with percentages. There were no differences between the groups in all parameters.

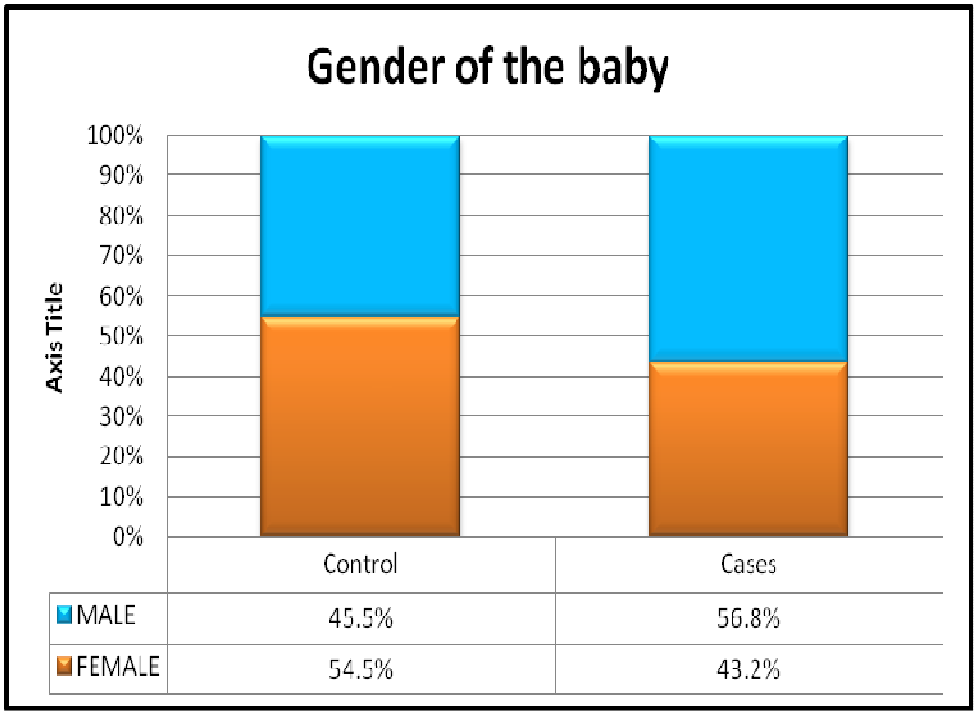


Chart 1: gender distribution in case and control group

Table 3: Comparison of albumin and bilirubin levels in cord blood and bilirubin at 24 and 72 hours of life between the control and case groups.

		N	Mean	Std. Deviation	Std. Error	
					Mean	P value
Mother' s age(years)	Control	55	24.91	2.933	.395	.078
	Cases	37	26.03	2.986	.491	.080
Birth Weight(kg)	Control	55	2.940	.3155	.0425	.517
	Cases	37	2.898	.2935	.0483	.511
Cord Sr.Albumin	Control	55	3.587	.6569	.0886	.842
	Cases	37	3.559	.6496	.1068	.842
Cord Total Sr. Bilirubin	Control	55	1.596	.4670	.0630	.025
	Cases	37	1.995	1.1638	.1913	.054
Cord Indirect Sr. Bilirubin	Control	55	1.391	.3831	.0517	.054
	Cases	37	1.697	1.0707	.1760	.102
Total Sr.Bilirubin at 24 hours of life	Control	55	7.571	3.3235	.4481	.406
	Cases	37	7.035	2.4940	.4100	.380
Indirect Sr.Bilirubin at 24 hours of life	Control	55	6.773	3.4620	.4668	.311
	Cases	37	6.105	2.4031	.3951	.278
Total Sr.Bilirubin at 72 hours of life	Control	55	12.384	3.0205	.4073	.069
	Cases	37	13.686	3.7483	.6162	.082
Indirect Sr.Bilirubin at 72 hours of life	Control	55	11.013	2.6942	.3633	.152
	Cases	37	11.957	3.5662	.5863	.176

The umbilical cord blood total bilirubin was significantly higher in babies with ABO incompatibility than the control group.

There was no statistically significant difference in other parameters between the groups.

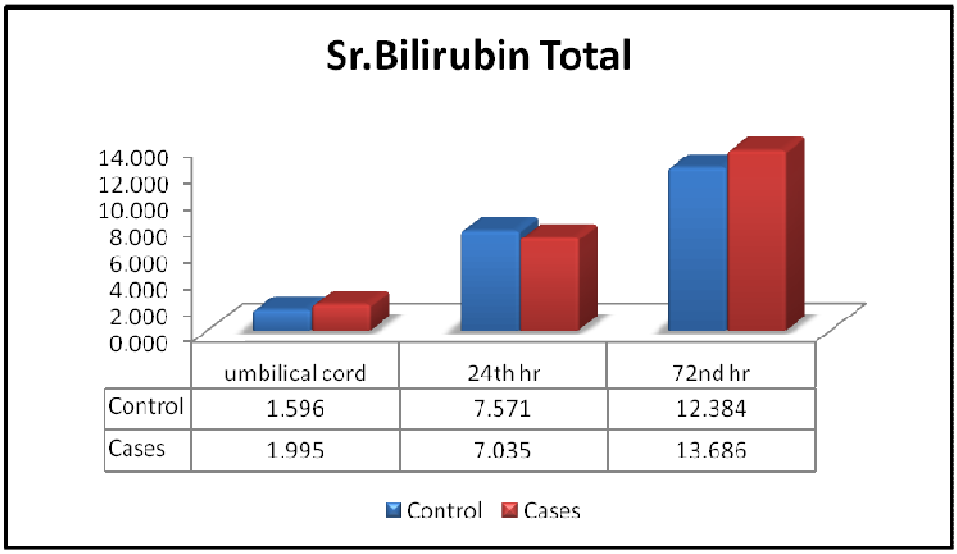


Chart 2: Comparison of mean total serum bilirubin levels in umbilical cord, at 24 and 72 hours of life between case and control groups

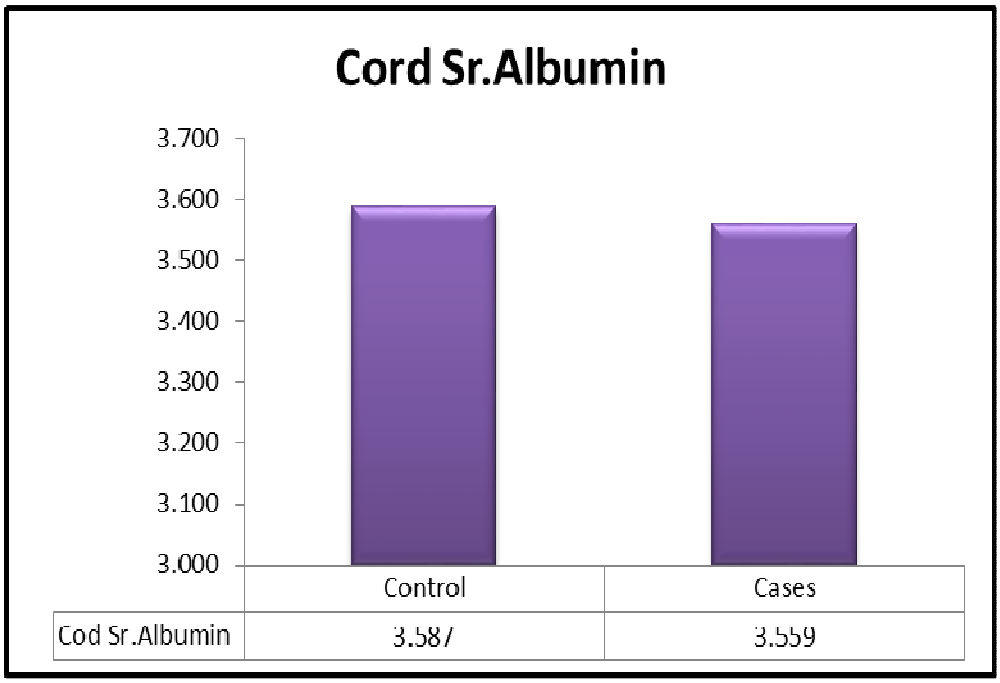


Chart 3: Comparison of umbilical cord Serum Albumin levels between case and control groups

Table 4: comparison of albumin and bilirubin levels in umbilical cord and bilirubin at 24 and 72 hours of life between male and female babies

	Sex of baby	N	Mean	Std. Deviation	Std. Error Mean	P val ue
Cord Sr.Albumin	Male	46	3.541	.6327	.0933	.611
	Female	46	3.611	.6730	.0992	.611
Cord Total Sr.Bilirubin	Male	46	1.802	.9323	.1375	.604
	Female	46	1.711	.7415	.1093	.605
Total Indirect Sr. Bilirubin	Male	46	1.554	.8482	.1251	.610
	Female	46	1.474	.6455	.0952	.610
Total Sr.Bilirubin at 24 hrs of life	Male	46	7.817	3.4170	.5038	.142
	Female	46	6.893	2.5019	.3689	.142
Indirect Sr.Bilirubin at 24 hrs of life	Male	46	7.039	3.6203	.5338	.096
	Female	46	5.970	2.3516	.3467	.097
Total Sr.Bilirubin at 72 hrs of life	Male	46	13.193	3.5337	.5210	.419
	Female	46	12.622	3.2199	.4748	.419
Indirect Sr.Bilirubin at 72 hrs of life	Male	46	11.541	3.3547	.4946	.647
	Female	46	11.243	2.8326	.4176	.647

There was no statistically significant difference in serum albumin and bilirubin levels in umbilical cord and Sr.bilirubin at 24 and 72 hours of life between the 2 sexes.

Table 5: Comparison of incidence of significant neonatal hyperbilirubinemia between the case and control group

			Control	Cases	Total
JAUNDICE	Absent	Count	46	29	75
		%	83.6%	78.4%	81.5%
	Present	Count	9	8	17
		%	16.4%	21.6%	18.5%
Total		Count	55	37	92
		%	100.0%	100.0%	100.0%

There is no statistically significant difference in incidence of neonatal hyperbilirubinemia between case and control group with a p value of 0.524 which is higher than 0.05.

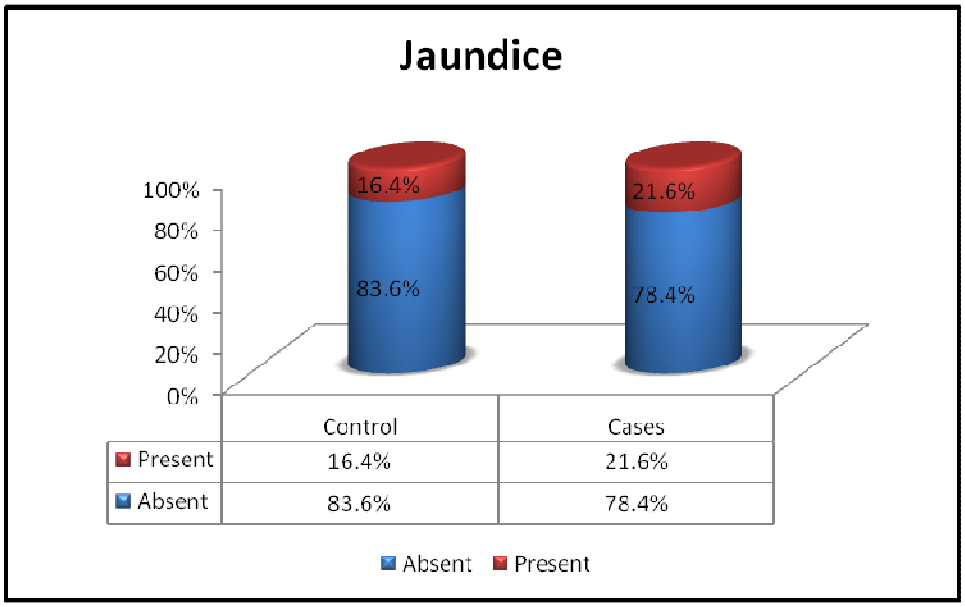


Chart 4: comparison of incidence of neonatal jaundice between case and control groups.

Table 6: Comparison of age at development of significant neonatal hyperbilirubinemia between the control and case group.

S. No	Parameter	Control (n=9)	Cases (n=8)	P value	Statistical test
1	Age of neonates (hours of life)	42.6 ± 23.3	45 ± 23.7	0.999 (NS)	Mann Whitney test
2	Proportion at 24 hours of life	5(55.5%)	4 (50%)	0.999 (NS)	Fisher's exact test

There was no statistically significant difference in age at development of significant neonatal hyperbilirubinemia between case and control group.

Table 7: Comparison of other parameters of the neonates who developed significant hyperbilirubinemia

S. No	Parameter	Control (n=9)	Cases (n=8)	P value	Statistical test
1	Hemoglobin (g/dl)	13.89 ± 0.78	13.5 ± 1.89	0.641	Unpaired 't' test
2	Peripheral smear				
	Normal	100%	100%	--------	--------
	Abnormal	0%	0%		
3	Exchange transfusion done				
	Yes	0 (0%)	2 (25%)	0.2 (NS)	Fisher's Exact test
	No	9 (100%)	6 (75%)		
4	RBC count (million/cc)	3.9 ± 0.7	3.4 ± 0.8	0.172 (NS)	Unpaired 't' test
5	Hematocrit (%)	45.1 ± 3.1	39.5 ± 4.2	0.006*	Unpaired 't' test

* indicates $P<0.05$ and is considered statistically significant.

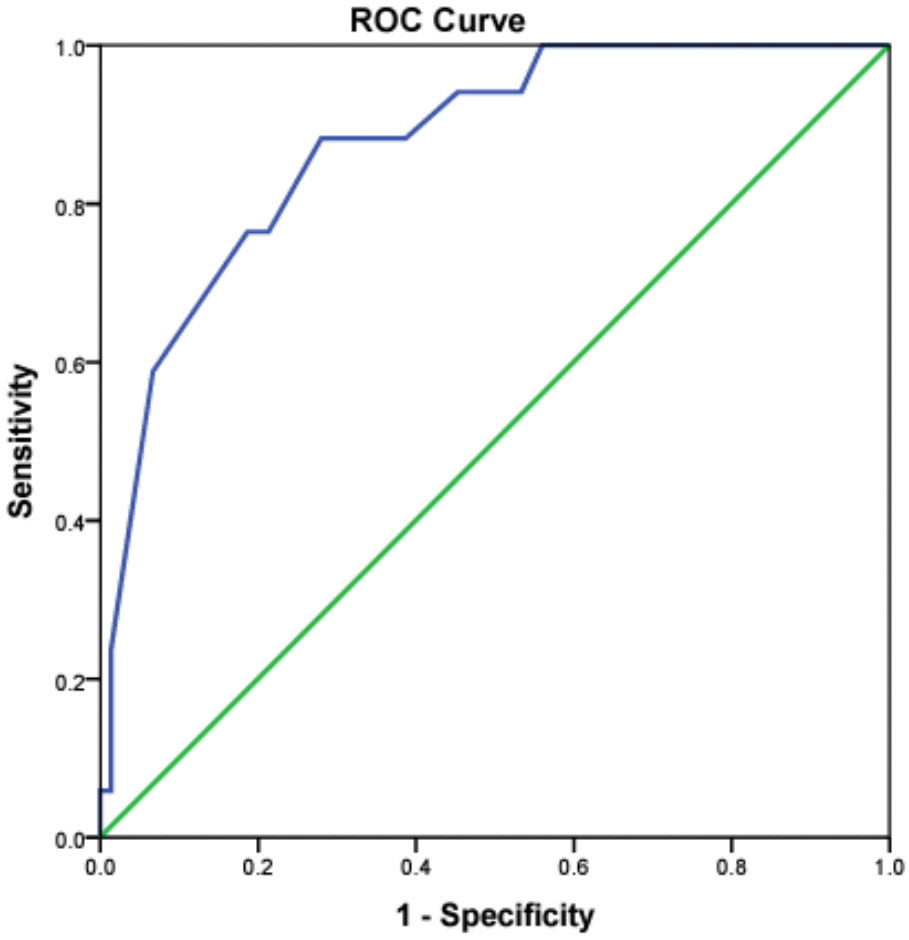
Data are expressed as mean ± SD except peripheral smear and exchange transfusion done wherein the data are expressed as absolute numbers with percentages.

Hematocrit in case group was significantly low when compared to control group.

DETERMINATION OF CUT OFF LEVEL FOR UMBILICAL CORD SERUM ALBUMIN FOR DEVELOPMENT OF SIGNIFICANT HYPERBILIRUBINEMIA AMONG VARIOUS GROUPS

FOR THE STUDY POPULATION

RECEIVER OPERATING CHARACTERISTIC CURVE TO ASSESS THE ABILITY OF CORD SERUM ALBUMIN TO PREDICT SIGNIFICANT HYPERBILIRUBINEMIA IN THE STUDY POPULATION



Diagonal segments are produced by ties.

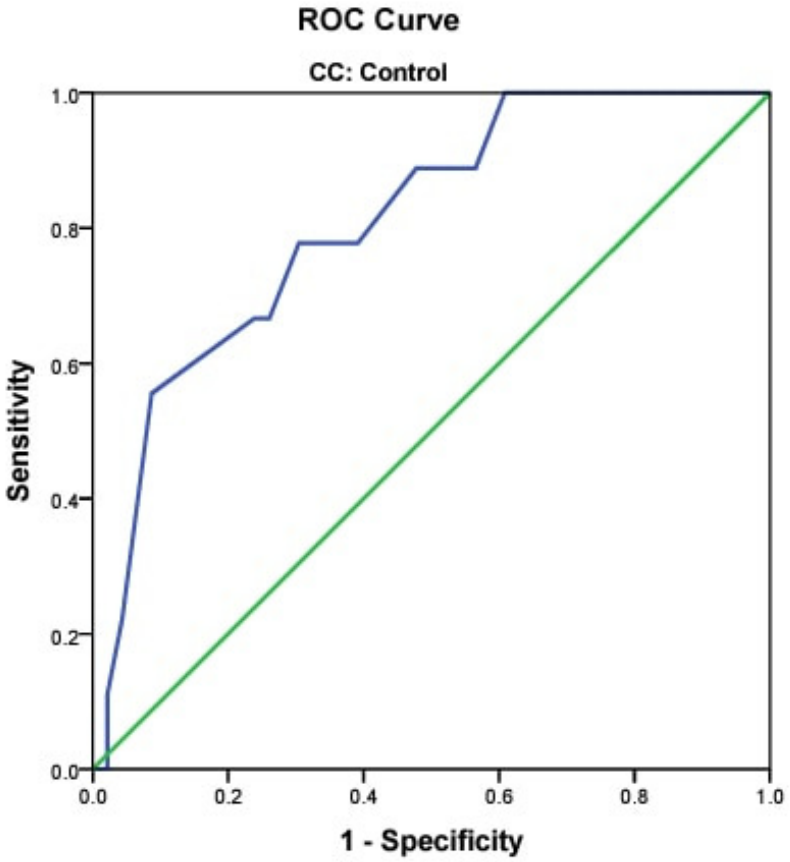
Table 8: Area under the curve for umbilical cord serum albumin in the study population

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.875	.043	.000	.791	.960

This table shows that umbilical cord albumin has a large area under the curve of 0.875 indicating its high predictive ability for significant hyperbilirubinemia.

FOR CONTROL GROUP:

ROC CURVE TO ASSESS THE ABILITY OF CORD SERUM ALBUMIN TO PREDICT SIGNIFICANT HYPERBILIRUBINEMIA IN THE CONTROL GROUP



Diagonal segments are produced by ties.

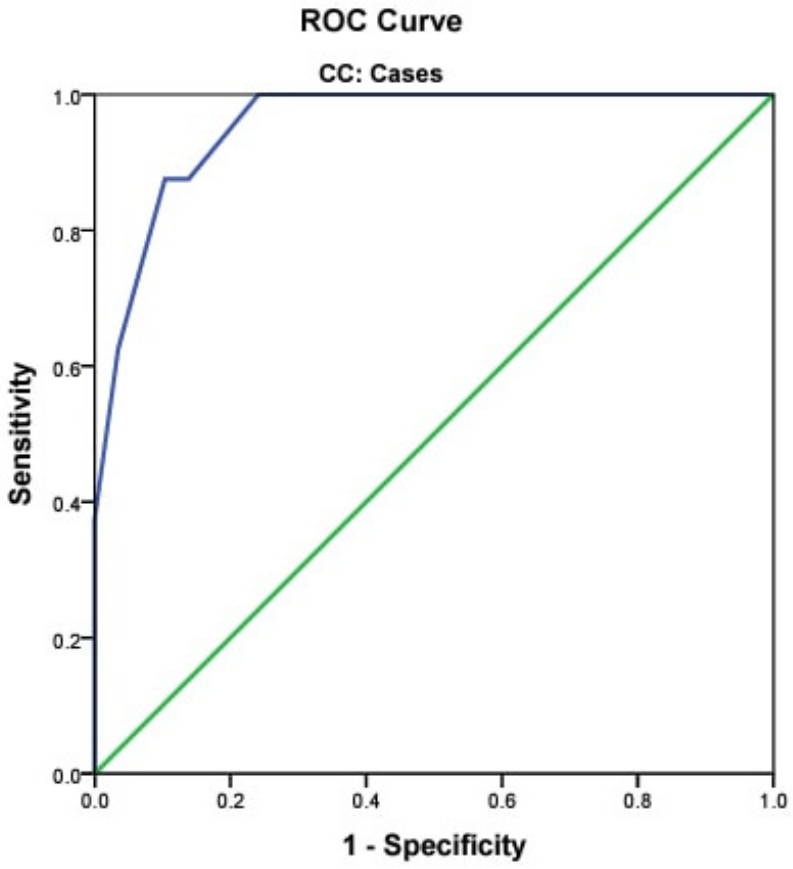
Table 9: Area under the curve for umbilical cord serum albumin in the control group

Area	Std. Error[b]	Asymptotic Sig.[c]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.809	.074	.004	.665	.953

This table shows that area under the curve for umbilical cord serum albumin for significant hyperbilirubinemia as .809.

FOR CASE GROUP:

ROC CURVE TO ASSESS THE ABILITY OF UMBILICAL CORD SERUM ALBUMIN TO PREDICT SIGNIFICANT HYPERBILIRUBINEMIA IN THE CASE GROUP



Diagonal segments are produced by ties.

Area Under the Curve[a]

Table 10: Area under the curve for umbilical cord serum albumin in the case group

Area	Std. Error[b]	Asymptotic Sig.[c]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.955	.032	.000	.892	1.000

This table shows that umbilical cord albumin has a large area under the curve of 0.955 indicating its high predictive ability for significant hyperbilirubinemia.

DETERMINATION OF CUT OFF LEVEL FOR UMBILICAL CORD SERUM TOTAL BILIRUBIN FOR DEVELOPMENT OF SIGNIFICANT HYPERBILIRUBINEMIA AMONG VARIOUS GROUPS

FOR STUDY POPULATION:

ROC CURVE TO ASSESS THE ABILITY OF UMBILICAL CORD SERUM TOTAL BILIRUBIN TO PREDICT SIGNIFICANT HYPERBILIRUBINEMIA IN THE STUDY POPULATION

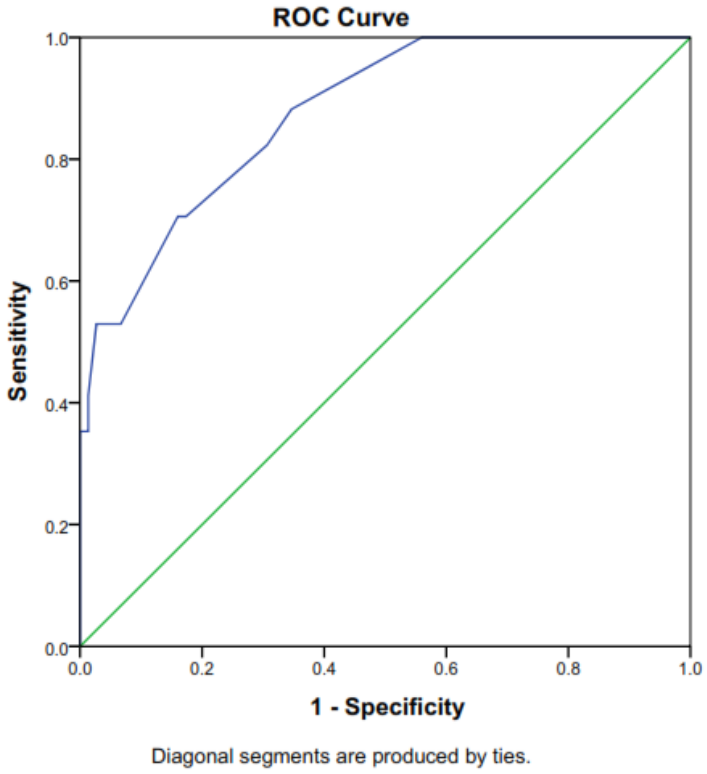


Table 11: Area under the curve for umbilical cord serum total bilirubin in the study population

Area	Std. Error[a]		Asymptotic 95% Confidence Interval	
		Asymptotic Sig.[b]	Lower Bound	Upper Bound
.876	.043	.000	.791	.961

This table shows that umbilical cord serum total bilirubin has a large area under the curve of 0.876 for prediction of significant hyperbilirubinemia at birth.

FOR CONTROL GROUP:

ROC CURVE TO ASSESS THE ABILITY OF UMBILICAL CORD SERUM TOTAL BILIRUBIN TO PREDICT SIGNIFICANT HYPERBILIRUBINEMIA IN THE CONTROL GROUP

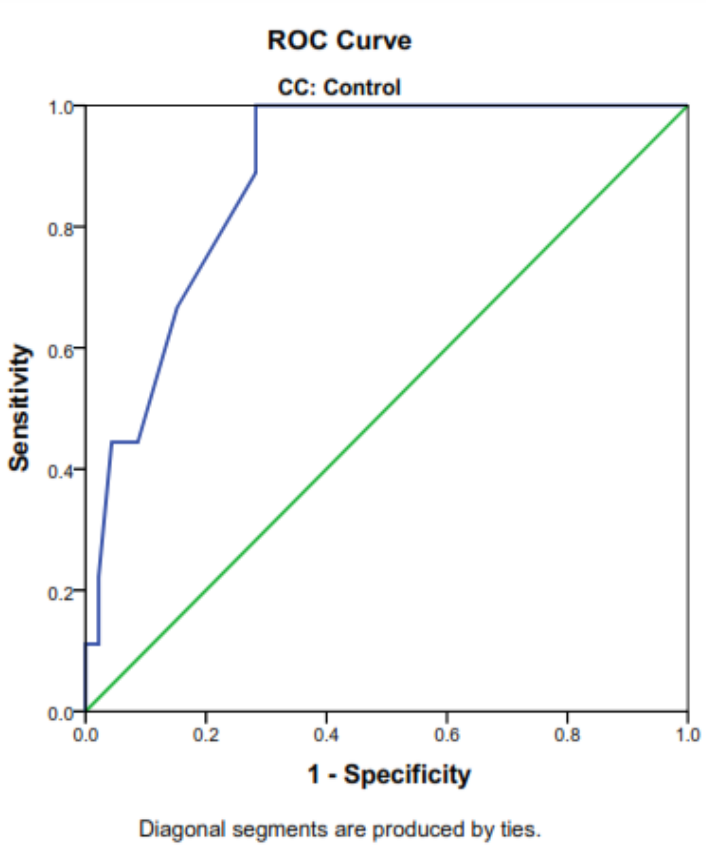


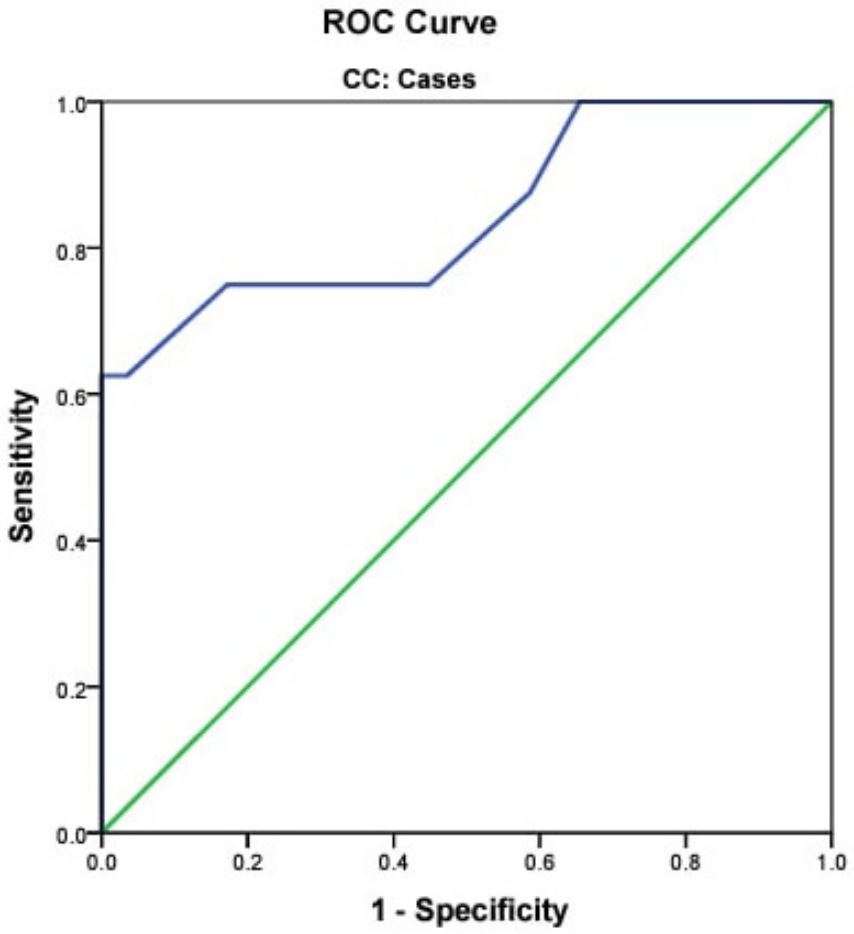
Table 12: Area under the curve for umbilical cord serum total bilirubin in control group

				Asymptotic 95% Confidence	
		Asymptotic		Interval	
Area	Std. Error[b]	Sig.[c]		Lower Bound	Upper Bound
.884	.047	.000		.792	.976

This table shows that umbilical cord serum total bilirubin has a large area under the curve of 0.884 for prediction of significant hyperbilirubinemia at birth in control group.

FOR CASE GROUP:

ROC CURVE TO ASSESS THE ABILITY OF UMBILICAL CORD SERUM TOTAL BILIRUBIN TO PREDICT SIGNIFICANT HYPERBILIRUBINEMIA IN THE CASE GROUP



Diagonal segments are produced by ties.

Area Under the Curve[a]

Table 13: Area under the curve for umbilical cord serum total bilirubin in control group

Area	Std. Error[b]	Asymptotic Sig.[c]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.845	.091	.003	.667	1.000

This table shows that the umbilical cord total bilirubin has an area under the curve of .845 for predicting significant hyperbilirubinemia in the control group.

DISCUSSION

100 neonates who fulfilled the inclusion and exclusion criteria were enrolled in the study. Out of the 100 babies, 4 babies who could not be followed up were excluded from the study. 3 babies who got admitted in the NICU for sepsis, neonatal seizures and respiratory distress were excluded from the study. Another baby, who on evaluation was found to have conjugated hyperbilirubinemia was also excluded from the study. The dropout rate was 8% and the remaining 92 neonates were followed up.

55 babies with blood group O+ve served as controls and 37 babies with blood group A+ve and B+ve served as cases. There was no statistically significant difference in the baseline demographic characteristics between the 2 groups.

The mean serum albumin level in the umbilical cord blood was 3.587 $\pm$0.65 g/dl in control and 3.559$\pm$0.64 g/dl in case group. There was no

statistically significant difference in mean serum albumin level in umbilical cord blood between the two groups.

The mean cord serum total bilirubin level was 1.995±1.16 mg/dl in cases, which is significantly higher than 1.596±.46 mg/dl in control group. This result was similar to Zietoun et al,(33) Aljabri et al(42) and Hamdi et al studies.(29) There was no stsatistically significant difference in mean serum bilirubin between the groups at 24 and 72 hours of life.

The mean serum total bilirubin at 24 hours of life was 7.571±3.32 mg/dl in control group and 7.035±2.49 mg/dl in case group.

The mean serum total bilirubin at 72 hours of life was 12.384±3.02 mg/dl in control group and 13.686±3.74 mg/dl group.

There was no statistically significant difference in serum bilirubin and albumin levels in cord between male and female babies. This results matched with Amar et al (28) and Rostami and Mehrabi studies. (43)

The incidence of significant hyperbilirubinemia was 16.45% in control group and 21.6% in case group. The overall incidence of significant hyperbilirubinemia in our study was 18.4%. This result correlates with Bernaldo AJNB and Segre CADM(35) and Nahar Z et al (31)studies who reported an incidence of 15% and 15.5% respectively. In our study, we did not observe any statistically significant difference in developing significant hyperbilirubinemia between the two groups. This may be due to the small sample size.

By ROC analysis, the cutoff point for umbilical cord serum albumin for development of significant hyperbilirubinemia for the study population was 3.15 g/dl. This value predicts the development of significant hyperbilirubinemia with a sensitivity of 76.5%, specificityof 78.7% and an accuracy of 77.6%. The area under the curve is 0.875, which shows its high predictive value. This value was lower when compared to other authors. Venkatamurthy M et al(37) study reported that umbilical cord serum albumin level $\geq$3.4 g/dl to be safe as none of the babies with CSA more than this value developed hyperbilirubinemia in their study.

Table 14: Comparison of cut-off values of umbilical cord blood albumin for prediction of significant hyperbilirubinemia with other authors

Sl no	Authors	Year	Results
1	Our study		≥3.15 g/dl
2	Venkatamurthy et al	2014	≥3.4 g/dl
3	Sandeepkumar et al	2016	≥3.4 g/dl
4	Suchanda et al	2017	≥3.3 g/dl

In control group, the cut-off value for umbilical cord blood albumin was 3.15g/dl with a sensitivity of 66.7%, specificity of 73.9% and an accuracy of 70.9%. In case group, a cut-off value of 3.15 g/dl predicts the development of significant hyperbilirubinemia with a high sensitivitity of 87.5%, specificity of 86.2% and a high accuracy rate of 86.9%. Thus, it was found that umbilical cord albumin has a high predictive value for significant hypebilirubinemia and the accuracy was high in babies with ABO incompatibility compared to controls.

By ROC analysis, the cut-off point for umbilical cord serum total bilirubin for development of significant hyperbilirubinemia for the study population was 1.85 mg/dl. This value predicts the development of significant hyperbilirubinemia with a sensitivity of 70.6%, specificity of 82.7% and an accuracy of 76.7%. The area under the curve was 0.876, which shows its high predictive value. While Rosenfeld J et al,(44) Hamdi et al (29) and Zietoun et al(33) study reported a cut off value of 2 mg/dl, 2 mg/dl and 2.15 mg/dl respectively. In control group, the cut-off value for umbilical cord blood albumin was 1.75 mg/dl with a sensitivity of 88.9%, specificity of 72% and an accuracy of 80.3%. In case group, a cut-off value of 1.85 mg/dl predicts the development of significant hyperbilirubinemia with a sensitivitity of 75%, specificity of 79.3% and accuracy rate of 77.2%.

Table 15: Comparison of cut-off values of umbilical cord bilirubin with various studies to predict neonatal hyperbilirubinemia

Sl. no.	Authors	year	Results
			Umbilical cord total serum bilirubin (predicts NNH)
1	Our study		>1.85 mg/dl
2	Robinson et al	1960	>3 mg/dl
3	Risemberg et al	1977	>4 mg/dl
4	Rosenfeld et al	1986	>2 mg/dl
5	Knudsen et al	1989	>2.33 mg/dl
6	Rataj J et al	1994	>2.5 mg/dl
7	Suresh and Clark	2004	>2 mg/dl
8	Bernaldo AJN and Segre CADM	2004	>2 mg/dl
9	Taksande A et al	2005	>2 mg/dl
10	Saltrya R et al	2009	$\geq$2.54 mg/dl
11	Rudy et al	2009	>2.54 mg/dl
12	Kanchanabat et al	2010	>2.3 mg/dl
13	Hamdi et al	2012	>2 mg/dl
14	Zeitoun et al	2013	>2.15 mg/dl in FT >2.05 mg/dl in PT
15	Trivedi et al	2013	$\geq$2.5 mg/dl
16	Menon et al	2016	$\geq$2 mg/dl

CONCLUSION

- In umbilical cord blood, the mean serum albumin and mean serum total bilirubin in babies with blood group O+ve born to O+ve mothers was 3.587±0.65 g/dl and 1.596±0.64 mg/dl respectively.
- In umbilical cord blood, the mean serum albumin and mean serum total bilirubin in babies with blood group A+ve and B+ve born to O+ve mothers was 3.559±0.64 g/dl and 1.995±1.16 mg/dl respectively.
- The umbilical cord serum albumin and total bilirubin correlates well with the development of significant neonatal hyperbilirubinemia requiring treatment in the form of phototherapy with or without exchange transfusion.
- Umbilical cord serum albumin level of less than or equal to 3.15 g/dl predicts the development of significant hyperbilirubinemia with a sensitivity of 76.5%, specificity of 78.7% and an accuracy of 77.6%.

- Umbilical cord serum total bilirubin of more than or equal to1.85 mg/dl predicts the development of significant hyperbilirubinemia with a sensitivity of 70.6%, specificity of 82.7% and an accuracy of 76.7%.

We recommend routine measurement of serum bilirubin and albumin levels in umbilical cord blood at birth and babies with total bilirubin >1.85 mg/dl and albumin $\leq$3.15 g/dl in ABO blood group incompatibility should be followed up closely to watch for the development of significant hyperbilirubinemia requiring treatment in the form of phototherapy with or without exchange transfusion while those babies with cord total bilirubin $\leq$1.85 mg/dl and albumin>3.15 g/dl can be safely discharged early.

SUMMARY

- 100 healthy term newborns born to O+ve mothers in Raja Mirasudhar Hospital attached to Thanjavur Medical College during the period of February 2017 to August 2017 were included in the study.

- Relevant clinical history was obtained from the mother and maternal hospital records. A complete clinical examination of the neonate was done at the time of birth.

- Blood grouping, Rh typing, Serum albumin and serum total bilirubin were estimated in the umbilical cord blood.

- The neonates were grouped into case and control group based on their blood group. Babies with blood group O+ve served as controls while those with A+ve and B+ve served as cases.

- The neonates were followed up daily for the development of significant hyperbilirubinemia and serum bilirubin was measured in all neonates at 24 and 72 hours of life.

- Development of significant hyperbilirubinemia requiring treatment in the form of phototherapy with or without exchange transfusion was taken as the major outcome of the study.

- By using Receiver Operating Curves ciut-off values for umbilical cord serum bilirubin and albumin for prediction of significant hyperbilirubinemia was calculated.

- The umbilical cord serum albumin and total bilirubin correlates well with the development of significant neonatal hyperbilirubinemia.

- In babies with ABO incompatibility umbilical cord serum total bilirubin $\geq$1.85 mg/dl and albumin $\leq$3.15 g/dl predict development of significant hyperbilirubinemia and should be closely followed up, while those babies with cord bilirubin $\leq$1.85 mg/dl and albumin $\geq$3.15 g/dl can be discharged early.

ANNEXURE -1

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41. Management of hyperbilirubinemia in the newborn infant 35 or more week of gestation. Pediatrics 2004Jul;114(1). Figure 4, Guidelines for exchange transfusion for hospitalized infants of 35 or more weeks' gestation.

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ANNEXURE 2

PROFORMA OF THE DISSERTATION

PREDICTIVE VALUE OF UMBILICAL CORD BLOOD BILIRUBIN AND ALBUMINN FOR SIGNIFICANT NEONATAL HYPERBILIRUBINEMIA IN ABO INCOMPATIBILITY

BABY OF: DOA:

SEX:

DOD:

DATE & TIME OF BIRTH:

BIRTH WEIGHT:

ASSESSMENT OF GESTATIONAL AGE:

METHOD	LMP	USG	NEW BALLORD SCORE
PERIOD OF GESTATION			

MATERNAL HISTORY:

BIRTH NOTES:

MODE OF DELIVERY-

APGAR AT 1 MIN-

5 MIN-

EXAMINATION OF BABY:

HEAD TO TOE EXAMINATION-

SYSTEM EXAMINAION-

INCLUSION CRITERIA:

CRITERIA	YES	NO
TERM BABIES >/=37 COMPLETED WEEKS		
MODE OF DELIVERY- NORMAL VAGINAL/C – SECTION		
BIRTH WEIGHT >/= 2.5 KG		
APGAR AT 1 MIN >/= 7/10		
BLOOD GROUP A /B +VE BORN TO O+VE MOTHERS		
BLOOD GROUP O+VE BORN TO O+VE MOTHERS		

CONTROL / CASE

EXCLUSION CRITERIA:

CRITERIA	YES	NO
PRETERM		
Rh INCOMPATIILITY		
AT RISK OF SEPSIS		
INSTRUMENTAL DELIVERY		
BIRTH ASPHYXIA		
RESPIRATORY DISTRESS		
DIRECT HYPERBILIRUBINEMIA		
SIGNIFICANT CONGENITAL ANOMALIES		
INFANT OF DIABETIC MOTHER		
MECONIUM STAINED AMNIOTIC FLUID		

INVESTIGATION:

	Umbilical cord	24 hours of life	72 hours life
Serum total bilirubin			
Serum indirect billirubin			
Serum albumin			
Blood grouping typing			

Hemoglobin

RBC count

Hematocrit

Examination of the baby on

Day 1-

Day 2-

Day 3-

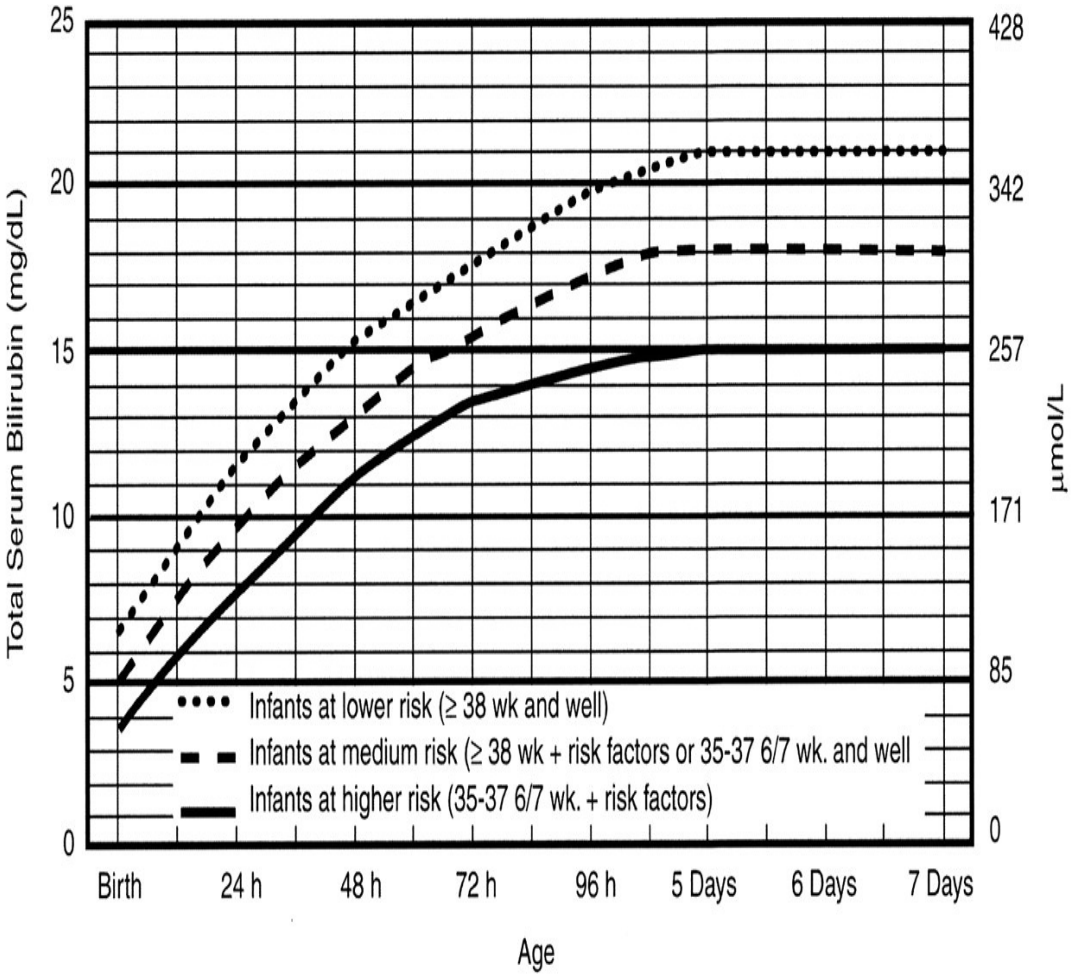
TREATMENT DETAILS:

PHOTOTHERAPY:

EXCHANGE TRANSFUSION

COURSE OF STAY IN NICU:

45.



- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin.
- Risk factors = isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis, or albumin < 3.0g/dL (if measured)
- For well infants 35-37 6/7 wk can adjust TSB levels for intervention around the medium risk line. It is an option to intervene at lower TSB levels for infants closer to 35 wks and at higher TSB levels for those closer to 37 6/7 wk.
- It is an option to provide conventional phototherapy in hospital or at home at TSB levels 2-3 mg/dL (35-50mmol/L) below those shown but home phototherapy should not be used in any infant with risk factors.

ANNEXURE - 3

CONSENT FORM

I hereby give consent for my child to participate in the study conducted by Dr.JANAKI.AN, post graduate in Department of Pediatrics, Thanjavur Medical College , Thanjavur – 613001 and to use my child'spersonal clinical data and result of investigation for the purpose of analysis and to study the nature of disease. I also give consent for further investigations.

Name of the participant :

Place:

Signature Of Parent

Date:

ANNEXURE 4

EXPLANATIONS FOR ABBREVIATIONS

TSB – Total Serum Bilirubin

TcB – Transcutaneous bilirubin

CSA – Umbilical cord serum albumin

CSB – Umbilical cord serum bilirubin

NNH – Neonatal hyperbilirubinemia

DAT – Direct Antibody Test

sl. No.	Name	Sex of baby	Mother' s age(years)	Mode of delivery	DOB	TOB	Birth Weight(kg)	Gestational Age	Baby Blood Group & Typing	umblical cord			24 hours of life		72 hours of life		jaundice	age at developmentof jaundice (hoursof life)	Sr.Bilirubin Mg/dl								hemoglobin g/dl	RBC Count (Million/cu MM)	hematocrit %	Peripheral Smear	number of days of Phototherapy	Exchange Transfusion
																			48 hours of life		72 hours of life		84 hours of life		96 hours of life							
								LMP		Sr.Albumin g/dl	Sr.Bilirubin Mg/dl		Sr.Bilirubin Mg/dl		Sr.Bilirubin Mg/dl																	
											Total	Indirect	Total	Indirect	total	Indirect			Total	Indirect	Total	Indirect	Total	Indirect	Total	Indirect						
1	B/Ojayasri	F	26	LSCS	7.2.2017	4.50PM	2.75	37 wk 1 d	O+ve	3.5	1.2	1	8.4	7.5	10.2	8	N															
2	B/Okrishnaven i	M	25	LSCS	10.2.17	9.30AM	3	39wk	A+ve	2.8	4.5	3.5	8.5	7.5	25.8	22.6	Y	72	14	13	26	23	20	17	18	15	13	2.5	40	Normal	3	Y
3	B/Opoornima	M	24	LSCS	6.2.17	10.15AM	3.1	38wk 5 d	O+ve	3.5	1.2	1	5.4	4	11	9.6	N															
4	B/OvellaiAmmal	F	28	LSCS	13.2.17	9.52AM	3.3	39wk 6 d	O+ve	2.5	2	1.8	8.5	7.5	6.6	5.6	N															
5	B/Opodhumalli	M	30	LSCS	14.2.17	10.05AM	2.9	39wk 4 d	B+ve	3.2	1.6	1.4	10	9	16		N															
6	B/Ochithiraiselvi	M	30	LSCS	15.2.17	10.00 AM	3.2	39wk	B+ve	3	2	1.8	3.1	2.7	10	9.6	N															
7	B/Osudha devi	M	25	LN	16.2.17	12.43PM	3.4	39wk 4 d	B+ve	2.7	6	5.8	11.2	10.2	19	18	Y	24	16	15	19	18	15	14	12	11	14	3	45	Normal	3	N
8	B/Onadhiya	M	27	LN	16.2.17	10.12PM	2.5	37wk 5 d	O+ve	3.5	2	1.6	8.6	7.2	12	11	N															
9	B/OShruthi	F	25	LN	17.2.17	12.11AM	2.75	40wk	O+ve	3.3	1.5	1.3	8.4	7.4	12.7	11.7	N															
10	B/Ojeeva	M	22	LSCS	16.2.17	10.15PM	2.54	37wk 2 d	O+ve	3.4	0.9	0.8	7.8	6.2	11.7	10.1	N															
11	B/Opunitha	M	26	LSCS	22.2.17	8.15PM	3.26	39wk 3 d	B+ve	2.4	4.2	3.6	14.8	13.8	14.2	11	Y	24	16	15	14	11					16	4	45	Normal	1	N
12	B/O abirAmi	M	25	LN	18.2.17	11.30AM	3.3	39wk 3 d	O+ve	3	1.6	1.4	6.6	5.6	12	11	N															
13	B/O kasthuri	M	21	LN	25.2.17	11.47AM	2.5	38wk 6 d	O+ve	3.2	2.4	2.1	8.2	7.2	12.9	11.9	N															
14	B/O Suganya	F	23	LSCS	25.2.17	9.24AM	2.8	39wk 5 d	O+ve	3	1.3	1.1	5	4	10	9	N															
15	B/Ojevitha	F	23	LSCS	26.2.17	2.32PM	3.4	39wk 3 d	O+ve	2.8	1.6	1.1	5.1	4.4	10	9	N															
16	B/O Sasikala	F	24	LN	26.2.17	5.16PM	2.75	40wk 3 d	O+ve	3	1	0.8	1.9	1.7	10	8.6	N															
17	B/O Satya	M	29	LSCS	27.2.17	5.23AM	2.7	39wk 2 d	O+ve	3.6	1.3	1.1	4.8	4.2	12.2	11	N															
18	B/O Rubini	F	26	LN	26.2.17	5.44PM	3	40wk 3 d	O+ve	4.5	1.4	1.1	5.1	4.3	10	9.5	N															
19	B/O Rajathi	F	20	LSCS	27.2.17	6.12AM	2.5	38wk	O+ve	3	1.8	1.4	6.2	5.9	11	10.2	N															
20	B/O marikannu	F	29	LSCS	27.2.17	9.30AM	2.8	38wk 3 d	O+ve	2.9	1.8	1.4	5.8	5	9.8	7	N															
21	B/O Kanimozhi	M	24	LSCS	31.3.17	8.55PM	3	39wk	A+ve	3	1.6	1.4	4.2	3.4	19.6	18.6	Y	48			20	19	18	17	12	11	13.4	4.51	40	NoMal	2	N
22	B/O GowthAm		26	LSCS	31.3.17	7.48PM	2.9	39wk 4 d	B+ve	4.2	1.8	1.5	7.7	6.5	13.8	12.2	N															
23	B/O ParAmeshwari	F	24	LSCS	8.4.17	10.30AM	2.75	39wk 2 d	O+ve	3.7	0.9	0.7	8.2	7.6	12	11	N															
24	B/O ThAmilarasi	M	22	LSCS	7.4.17	10.30AM	3.4	38wk 1 d	O+ve	3.6	1.6	1.3	7	6.1	9.6	8.5	N															
25	B/O Paulin anthony mary	M	24	LSCS	8.4.17	9.40AM	3	39wk 1 d	O+ve	2.9	1.1	1.3	9	8	12.5	11.5	N															
26	B/O Devi twin 1	M	23	LSCS	7.5.17	2.28PM	2.5	39wk 5 d	B+ve	3.4	1.3	1.1	4.5	3.5	9.2	8.2	N															
27	B/O Devi twin 2	M	23	LSCS	7.5.17	2.29PM	2.5	39wk 5 d	B+ve	2.8	0.9	0.8	4.4	3.4	9.2	8	N															
28	B/O mariAmmal	M	24	LN	2.5.17	2.05PM	3.5	37wk 6 d	B+ve	3.2	1.5	1.3	13.8	12.6	12.6	10.2	Y	24	16	14	13	10					15	3.42	34	Normal	1	N
29	B/O Thilagavathy	F	24	LSCS	2.5.17	5.55PM	3	40wk 1 d	O+ve	3.5	1.1	1.3	7.4	6.8	11.3	10.3	N															
30	B/O Nishanthini	F	24	LSCS	2.5.17	4.58PM	3.5	38wk 5 d	B+ve	3.2	1.5	1.2	4.6	3.8	12	11.2	N															

sl. No.	Name	Sex of baby	Mother' s age(years)	Mode of delivery	DOB	TOB	Birth Weight(kg)	Gestational Age	Baby Blood Group & Typing	umblical cord			24 hours of life		72 hours of life		jaundice	age at developmentof jaundice (hoursof life)	Sr.Bilirubin Mg/dl								hemoglobin g/dl	RBC Count (Million/cu MM)	hematocrit %	Peripheral Smear	number of days of Phototherapy	Exchange Transfusion
																			48 hours of life		72 hours of life		84 hours of life		96 hours of life							
								LMP		Sr.Albumin g/dl	Sr.Bilirubin Mg/dl		Sr.Bilirubin Mg/dl		Sr.Bilirubin Mg/dl				Total	Indirect	Total	Indirect	Total	Indirect	Total	Indirect						
											Total	Indirect	Total	Indirect	total	Indirect															
31	B/O Kaviyarasi	M	23	LSCS	18.4.17	11.15AM	2.5	39wk	B+ve	3.4	1.4	1.1	5.8	4.9	13.8	11.4	N															
32	B/O malathy	M	28	LSCS	18.5.16	25.4.17	2.7	39wk	O+ve	3	1	1.3	3.1	2.4	12.8	11.4	N															
33	B/O m ALA	F	24	LSCS	8.4.17	10.35AM	3.1	37wk 1 d	A+ve	3.3	1.2	0.8	6.2	6.4	10.5	9.5	N															
34	B/O Saranya	M	24	LSCS	7.5.17	1.12PM	2.5	40wk	B+ve	3.4	1.7	1.1	8.2	7	11.8	9.8	N															
35	B/O Saranya	M	23	LSCS	11.5.17	10.38AM	3.1	40wk	O+ve	4.8	1.3	1.1	7	6.5	14.9	13.3	N															
36	B/O Priyadharshini	M	21	LSCS	12.5.17	9.31AM	2.75	39wk 3 d	O+ve	4	1.3	1.1	5.6	4.9	11	10	N															
37	B/O Gayathri	F	22	LSCS	8.5.17	11.44AM	2.75	39wk	O+ve	2.8	2.5	2.2	11.8	10.4	14.6	13.2	Y	48	22	20	15	13							13.8	3.91	45.5	Normal	2	N
38	B/O Chitra	M	24	LSCS	9.5.17	10.58AM	3	39wk 3 d	O+ve	4.6	1.3	1	7.4	6.4	11	10	N															
39	B/O Satya	F	28	LSCS	10.5.17	9.24AM	3	39wk 4 d	O+ve	4.4	1.6	1.3	4.8	3.8	8.8	7.6	N															
40	B/O Prabhavathy	M	27	LSCS	8.5.17	9.46AM	3.5	38wk 5 d	O+ve	4.1	2.6	2.3	9.2	8.2	11.6	10.5	N															
41	B/O madhavi	M	24	LSCS	8.5.17	12.37PM	3	38wk 6 d	O+ve	3.8	1.3	1.2	9.4	8.4	15	14	N															
42	B/O Sudha	M	26	LSCS	6.5.17	10.06AM	3	39wk	O+ve	3.4	1.4	1.3	8.2	17.2	12.8	11.7	N															
43	B/O Kalaivani	F	21	LSCS	4.5.17	10.26AM	3.5	39wk 1 d	O+ve	3.1	1.2	1.3	6	5.1	11.2	10.2	N															
44	B/O manju parkavi	F	28	LSCS	5.5.17	10.15AM	2.5	39wk 2 d	O+ve	4.2	1.8	1.3	6.7	5.9	12.2	11.2	N															
45	B/O Sudha	M	26	LSCS	12.5.17	5.22PM	2.8	39wk 4 d	A+ve	4	1.7	1.5	6.8	5.8	12	10.8	N															
46	B/O Sarala	M	22	LSCS	13.5.17	1.00PM	3	40wk 5 d	B+ve	3.6	1.6	1.2	7.4	6.3	10.3	8.3	N															
47	B/O Elakkia	F	26	LSCS	13.5.17	10.55AM	3	39wk 6 d	O+ve	4.4	1.1	1.3	4	3.2	13	12	N															
48	B/O Praveena	F	26	LSCS	18.5.17	11.27AM	3	39wk	A+ve	3.2	1.9	1.7	8.2	7.3	13	12	N															
49	B/O Ambika	F	26	LSCS	11.6.17	3.07PM	3.2	41wk 1 d	B+ve	3.8	1.6	1.3	8	7	12	11	N															
50	B/O Podhumselvi	M	32	LSCS	29.5.17	3.25PM	3.25	38wk	B+ve	3.6	1.8	1.4	7.8	6.8	12	10.8	N															
51	B/O Bhavani	F	21	LSCS	2.6.17	10.40AM	2.51	39wk 3 d	O+ve	3.2	2	1.6	6	5.6	12.4	11.3	N															
52	B/O Aswini	F	24	LSCS	3.6.17	9.29AM	2.8	41wk	O+ve	3.4	1.3	1.1	7.1	6.9	11.2	10.9	N															
53	B/O Saranya	F	23	LSCS	10.6.17	10.1AM	3	39wk 2 d	O+ve	3.7	1.5	1.3	6	5.1	11	10	N															
54	B/O Ambika	F	24	LSCS	11.6.17	3.07PM	3.2	38wk 6 d	O+ve	3.2	2	1.8	16.8	15.7	12	11	Y	24	15	14	12	11							14	4.03	44.6	Normal	2	N
55	B/O Sivaranjani	F	22	LSCS	12.6.17	12.47PM	2.8	38wk 3 d	B+ve	2.8	2	1.8	7.2	6	19	17	Y	24	17	15	19	17			13	11			10.1	3.22	33.6	Normal	3	N
56	B/O RAmya	F	24	LSCS	13.6.17	5.25PM	2.7	38wk 5 d	B+ve	3.8	0.9	0.8	4	3.2	10	9	N															
57	B/O mala	M	25	LSCS	15.6.17	1.14AM	3.3	40wk 3 d	O+ve	4.2	1.5	1.3	3.5	2.7	10	9	N															
58	B/O Radhika	F	25	LSCS	12.6.17	10.05AM	3.2	39wk	O+ve	2.9	2	1.6	8.9	6.9	7.7	6.2	Y	24	17	15	8	6							14.2	4.88	49.3	Normal	2	N
59	B/O mahalakshmi	M	23	LSCS	15.6.17	10.10AM	3	39wk 3 d	O+ve	3.6	1.5	1.3	9.8	8.5	14	13	N															
60	B/O Ariyalakshmi	M	24	LSCS	19.6.17	7.45PM	2.5	40wk 2 d	O+ve	3.7	2.4	2.2	8.1	6.4	18.8	16.8	Y	72			19	17	16	15					14	4.2	45	Normal	2	N
61	B/O Pulikodi	F	23	LSCS	23.6.17	10.45AM	3.2	39wk	O+ve	4.3	1.8	1.3	5.8	4.6	12	10	N															

sl. No.	Name	Sex oF baby	Mother' s age(years)	Mode of delivery	DOB	TOB	Birth Weight(kg)	Gestational Age	Baby Blood Group & Typing	umblical cord			24 hours of life		72 hours of life		jaundice	age at developmentof jaundice (hoursof life)	Sr.Bilirubin Mg/dl									hemoglobin g/dl	RBC Count (Million/cu MM)	hematocrit %	Peripheral Smear	number of days of Phototherapy	Exchange Transfusion
																			48 hours of life		72 hours of life		84 hours of life		96 hours of life								
								LMP		Sr.Albumin g/dl	Sr.Bilirubin Mg/dl		Sr.Bilirubin Mg/dl		Sr.Bilirubin Mg/dl																		
											Total	Indirect	Total	Indirect	total	Indirect			Total	Indirect	Total	Indirect	Total	Indirect	Total	Indirect						
62	B/O Sugapriya	F	23	LSCS	23.6.17	9.37AM	3.25	40wk 1 d	O+ve	4	1	1.3	6.8	5.6	11	9.6	N																	
63	B/O AnjAmmal	F	24	LSCS	23.6.17	10.01AM	3	39wk 6 d	B+ve	4.7	1.2	1	6.2	5	13	11.6	N																	
64	B/O Loordusofia	F	30	LSCS	24.6.17	10.15AM	3.1	40wk 1 d	O+ve	4.4	1.3	1	7.3	5.5	14	12	N																	
65	B/O RevaTHI	F	29	LSCS	24.6.17	11.37AM	2.5	40wk	O+ve	4	1.5	1.3	2.4	2	16.1	13.2	N																	
66	B/O Sangeetha	F	30	LSCS	24.6.17	12.10PM	2.5	39wk	A+ve	4.2	1.4	1.2	6	5.8	12	11.6	N																	
67	B/O Parimala	F	34	LSCS	5.7.17	11.37AM	2.7	38wk 3 d	O+ve	3.5	2.8	2.4	11.3	9.8	16.6	14	Y	24	18	16	17	14							12	2.46	38	Normal	2	N
68	B/O Alagumathy	M	25	LSCS	6.7.17	9.52AM	3	40wk 2 d	A+ve	4.2	1.7	1.5	5.3	4.6	10.5	9.2	N																	
69	B/O Jeya	F	30	LSCS	7.7.17	12.25PM	3	38wk 5 d	O+ve	4.4	1.5	1.3	9	8.7	14.8	13.1	N																	
70	B/O Chitirai chelvi	M	24	LSCS	8.7.17	10.00AM	2.5	39wk	A+ve	4.2	1	0.8	7.2	7	11..2	10	N																	
71	B/O Bhuvaneshwari	F	27	LSCS	8.7.17	9.25AM	3	40wk 6 d	A+ve	4.6	1.4	1.1	4.7	3.4	11	10	N																	
72	B/O ShyAmala	M	25	LSCS	11.7.17	11.23AM	2.75	39wk 1 d	O+ve	3	1.8	1.6	10	9.8	21.8	19	Y	72			22	19			13	11	14	4.3	45	Normal	2	N
73	B/O Ambika	M	31	LSCS	12.7.17	12.45PM	3	39wk 6 d	O+ve	2.9	1.8	1.2	18	16	8.3	7.3	Y	24	19	17	8	7					14	3.24	45	Normal	2	N
74	B/O Sundari	F	32	LSCS	12.7.17	9.28AM	3.1	40wk 2 d	A+ve	3	3	2.6	6	5	22.8	19.5	Y	72			23	20	17	14	25	21	12	2.42	38	Normal	4	Y
75	B/O Vijayalakshmi	M	25	LSCS	10.7.17	10.47AM	3.6	38wk 2 d	O+ve	3.6	1	1.3	4	3	6	5	N																	
76	B/O VijayaF	F	28	LSCS	15.7.17	10.59AM	2.8	40wk 4 d	B+ve	4.6	2	1.5	7	6.5	13	12	N																	
77	B/O Saranya	F	28	LSCS	17.7.17	9.30AM	2.75	40wk	B+ve	3.8	1.8	1.6	4.5	3.5	11	10	N																	
78	B/O muthulakshmi	M	24	LSCS	20.7.17	10.37AM	3.5	39wk 1 d	O+ve	2.9	1.7	1.4	19.6	18.3	15	14	y	24	20	18	15	14					15	4.3	46	Normal	2	N
79	B/O Vanaroja	F	23	LSCS	10.7.17	9.30AM	2.5	39wk	A+ve	3.5	1.1	0.9	10.2	8.2	17	14.8	N																	
80	B/O Saritha	M	33	LSCS	10.7.17	9.35AM	3	39wk	A+ve	4	1.5	1.2	6	5	14	13	N																	
81	B/O mariAm beevi	M	21	LSCS	20.8.17	12.00AM	2.6	39wk 1 d	O+ve	3	1.8	1.3	9.7	8.7	14.8	12.8	N																	
82	B/O Devi	M	20	LSCS	21.8.17	11.05AM	2.6	38wk 2 d	O+ve	4.8	1.8	1.3	6.8	5.8	12	11	N																	
83	B/O Nathiya	M	25	LSCS	21.8.17	1.00AM	2.75	39wk 4 d	A+ve	3.1	1.8	1.6	7	6	14	13	N																	
84	B/O Sudha	M	25	LSCS	21.8.17	10.04AM	3	38wk 6 d	B+ve	3	2	1.8	7	6	12.5	11.4	N																	
85	B/O Dayana florence	F	24	LSCS	21.8.17	2.55PM	3.5	39wk 3 d	O+ve	3	1	1.3	7.8	6.4	16.2	14.2	N																	
86	B/O Regina devi	F	26	LSCS	21.8.17	4.10PM	2.75	37wk 5 d	O+ve	2.6	2.4	2.1	9.4	7.8	20.5	17.2	Y	72			21	17	18	17	12	11	14	4.42	48	Normal	2	N
87	B/O Dhivya	F	25	LSCS	21.8.17	7.50PM	2.5	37wk 5 d	O+ve	4.6	2.2	2	6.7	5.7	12	11	N																	
88	B/O Nagavalli	F	28	LSCS	22.8.17	6.54AM	2.4	37wk 3 d	B+ve	2.6	5.4	4.7	6.8	5.8	18	16.8	Y	72	16	15	18	17	12	11			15	4.44	40	Normal	3	N
89	B/O Swathiya	M	30	LSCS	21.8.17	8.20PM	2.75	40wk 2 d	B+ve	4.2	1.6	1.4	7.1	6.1	12.6	11.3	N																	
90	B/O Nandini	M	27	LSCS	22.8.17	9.00PM	3	37wk 2 d	O+ve	5.4	2.1	1.9	5	4	16.5	14.5	N																	
91	B/O Rajeshwari	F	29	LSCS	22.8.17	6.05AM	2.9	38wk 4 d	B+ve	4.4	2.2	2	5.8	4.8	15	14	N																	
92	B/O Vennila	F	23	LSCS	23.8.17	5.50AM	2.75	39wk 4 d	A+ve	4.8	2	1.8	7.1	6.1	10.4	9.4	N																	